

## **INHALTSVERZEICHNIS**

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# **1 Verzeichnis der Abkürzungen**

|             |                                                                             |
|-------------|-----------------------------------------------------------------------------|
| ABC         | ATP-Binding Cassette                                                        |
| AGATE       | Arbeitsgemeinschaft „Arzneimitteltherapie bei psychiatrischen Erkrankungen“ |
| AMÜP-Bayern | Arzneimittelüberwachung in der Psychiatrie Bayern                           |
| ATP         | Adenosintriphosphat                                                         |
| ATPase      | Adenosintriphosphatase                                                      |
| BCRP        | Breast-Cancer-Resistance-Protein                                            |
| BHS         | Blut-Hirn-Schranke                                                          |
| CYP         | Cytochrom P450                                                              |
| Da          | Dalton                                                                      |
| DNA         | Desoxyribonukleinsäure                                                      |
| GIT         | Gastrointestinaltrakt                                                       |
| GST         | Glutathion-S-Transferase                                                    |
| kD          | Kilo-Dalton                                                                 |
| MDD         | Major Depressive Disorder                                                   |
| MDR         | Multi Drug Resistance                                                       |
| MRP         | Multidrug-Resistance-related-Protein                                        |
| NAT         | N-Acetyltransferase                                                         |
| PEM         | Prescription-Event-Monitoring                                               |
| P-gp        | P-Glykoprotein                                                              |
| SULT        | Sulfotransferase                                                            |
| TDM         | Therapeutisches Drug Monitoring                                             |
| TMT         | Thiolmethyltransferase                                                      |
| TPMT        | Thiopurin-S-Methyltransferase                                               |

|     |                                  |
|-----|----------------------------------|
| UAW | unerwünschte Arzneimittelwirkung |
| UGT | Glucuronosyltransferase          |
| WHO | World Health Organisation        |
| WW  | Wechselwirkungen                 |

## **2 Einleitung**

### **2.1 Bedeutung von Wechselwirkungen (WW) von Arzneimitteln**

Das steigende Lebensalter<sup>1</sup> der Bevölkerung ist einer der Gründe für eine zunehmende Zahl an nebeneinander eingenommenen Medikamenten (Polypharmakotherapie), da Senioren (laut WHO „Alter“ ab dem 65. Lebensjahr<sup>2</sup>) oft multimorbide sind (paralleles Auftreten mehrerer Erkrankungen). Zu den Krankheiten, bei denen am häufigsten Polypharmakotherapie angewandt wird, zählen: Herzinsuffizienz, Diabetes mellitus, Hypertonie, Koronare Herzkrankheit und chronisch obstruktive Lungenerkrankungen<sup>3</sup>. Außer geriatrischen Patienten sind beispielsweise auch Aids- und Tumorpatienten und Diabetiker von der Polypharmakotherapie betroffen<sup>4</sup>.

Weitere Gründe für Polypharmakotherapie sind die ständig verbesserten diagnostischen Möglichkeiten und die steigende Zahl zur Verfügung stehender Präparate. Die Polypharmakotherapie (laut WHO ab fünf verschiedenen Medikamenten so bezeichnet, siehe auch 1. Heilmittelinformation vom September 2006) wird aber auch durch mangelnde Kommunikation zwischen verschreibenden Ärzten verursacht. Die zunehmende Anzahl von Lifestyle-Medikamenten zur Verbesserung des Wohlbefindens oder zur Leistungssteigerung (z.Bsp. Anti-Aging), obwohl medizinisch nicht immer indiziert, spielt sicherlich auch eine Rolle<sup>5</sup>. Bei mindestens 30%<sup>6</sup> der medikamentös behandelten Patienten kann man eine Polypharmakotherapie feststellen.

Die Anzahl der verschriebenen Medikamente, und damit auch der Wirkstoffe, nimmt mit dem Alter zu:

Laut einer Studie erhielten 13,4% der 61- bis 70-jährigen 13 Wirkstoffe und mehr, in der Altersgruppe über 90 Jahre waren es 30,5%.<sup>7</sup>

Das Risiko für unerwünschte Arzneimittelwirkungen (UAW) steigt mit der Anzahl der eingenommenen Medikamente hyperbolisch an (d.h. mit jedem neuen Medikament kommt nicht nur eine neue UAW dazu, sondern mehrere UAW):

Bei zwei eingenommenen Medikamenten beträgt das Risiko für UAW 13%, bei sieben Medikamenten beträgt es bereits 82%.<sup>8</sup>

Eine Wechselwirkung (Interaktion) ist per definitionem eine Veränderung der pharmakologischen Wirkung einer Substanz durch eine zweite Substanz, in quantitativer oder qualitativer Hinsicht<sup>9</sup>.

Je mehr verschiedene Medikamente ein Patient einnimmt, desto wahrscheinlicher ist eine Wechselwirkung zwischen den Präparaten<sup>10</sup>; bei zwei parallel verabreichten Medikamenten traten bei 0,17% der Patienten durch WW schwere Nebenwirkungen auf, bei 0,67% mäßige Nebenwirkungen. Bei acht oder mehr verabreichten Medikamenten waren es 3,58% schwere und 21,5% mäßige Nebenwirkungen.

Laut der Bundesvereinigung deutscher Apothekerverbände sind heute etwa 5000 Wechselwirkungen bekannt (ABDA, 26. Juni 2007).

Diese Interaktionen werden unterteilt in erwünscht/unerwünscht und die unerwünschten Wechselwirkungen wiederum in unterschiedliche Schweregrade<sup>11</sup>:

- **Schwerwiegend:** Mögliche Lebensgefährdung, Intoxikation (Vergiftung) oder bleibende Schäden, daher ist im Allgemeinen von einer gleichzeitigen Medikation abzusehen.
- **Mittelschwer:** Therapeutische Schwierigkeiten, daher ist eine Überwachung und Dosisanpassung bei gleichzeitiger Medikation durchzuführen.
- **Geringfügig:** Leicht verstärkte/verminderte Wirkung oder bei einem bestimmten Patientenkreis auftretende Wechselwirkungen (z.Bsp. Patienten mit Niereninsuffizienz).

- **Unbedeutend:** Keine/geringe Auswirkungen bei gleichzeitiger Medikation, in der Regel müssen keine Maßnahmen ergriffen werden.

Wechselwirkungen lassen sich auch nach ihrem Entstehungsmechanismus unterscheiden<sup>12</sup>:

### 2.1.1 Pharmakodynamische Wechselwirkungen

Zwei Wirkstoffe greifen synergistisch oder antagonistisch an demselben Rezeptor oder einem anderen Erfolgsorgan an<sup>13</sup>. Dabei gelten verschiedene Prinzipien<sup>14</sup>:

- **Agonisten-Antagonisten-Prinzip:** die Wirkstoffe konkurrieren aufgrund ihrer Affinität um den Rezeptor und modulieren seine Wirkung.
- **Agonisten-Agonisten-Prinzip:** die Wirkstoffe haben einen agonistischen Effekt auf den Rezeptor und addieren sich in ihrer Wirkung.

### 2.1.2 Pharmakokinetische Wechselwirkungen<sup>15</sup>

- **Veränderung der gastrointestinalen Resorption gleichzeitig verabreichter Stoffe:**

Zum Beispiel führt die Gabe von Metoclopramid zu einer beschleunigten Darmassage. Dies hat eine Resorptionsminderung von Digoxin zur Folge, da Digoxin nicht mehr lange genug mit der Resorptionsfläche des Darms in Kontakt ist<sup>16</sup>.

- **Verdrängung aus der Plasma-Protein-Bindung:**

Dies führt zu einem Konzentrationsanstieg des freien Anteils eines Wirkstoffes, was zu einer Überdosierung führen kann, ein Beispiel hierfür ist die Verdrängung von Bilirubin aus der Albuminbindung durch Salicylate<sup>17</sup>.

## **- Beeinflussung der Arzneimittelmetabolisierung und -elimination:**

- a) Beeinflussung des **hepatischen** Arzneimittelstoffwechsels: Cumarine beispielsweise werden überwiegend in der Leber über die Cytochrom-Enzymsysteme CYP3A4 und CYP2C9 abgebaut. Hemmstoffe dieser Enzymsysteme, wie zum Beispiel Cimetidin, führen zu einem verlangsamten Abbau von Cumarinen und zu einer Anreicherung nach wiederholter Einnahme<sup>18</sup>.
- b) Beeinflussung der **renalen** Elimination: Nichtsteroidale Antirheumatika, wie zum Beispiel Diclofenac, hemmen die Prostaglandinsynthese, wodurch die Nierendurchblutung und damit die glomeruläre Filtrationsrate erniedrigt sind, dies führt zum Beispiel zu einer verzögerten Ausscheidung von Lithiumsalzen und damit zu erhöhten Lithiumserumspiegeln<sup>19</sup>.
- c) Interaktion am **ABC-Transportprotein**<sup>20</sup>: Der bekannteste ABC-Transporter ist das P-Glykoprotein (P-gp). Als P-gp-Substrat dringt Loperamid kaum durch die Blut-Hirn-Schranke (BHS), weil es durch P-gp wieder aktiv in das Blut sezerniert wird. Daher wirkt Loperamid nur peripher und hat in der Regel keine unerwünschten zentralnervösen Effekte. Bei gleichzeitiger Anwendung mit einem P-gp-Inhibitor wie Chinidin kann es jedoch zu verstärkt auftretenden zentralnervösen Effekten wie zum Beispiel Atemdepression kommen<sup>21</sup>.
- Ein weiteres Beispiel für eine Barriere im Körper ist der Gastrointestinaltrakt (GIT). Hier vorhandenes P-gp sezerniert Substanzen ins Darmlumen und verhindert so die Aufnahme von Wirkstoffen. Substrate von P-gp wie z.Bsp. Talinolol, erreichen daher nur geringe Plasmakonzentrationen<sup>22</sup>.

## **- Beeinflussung der bakteriellen Darmflora durch Antibiotika:**

Breitbandantibiotika, wie z.Bsp. Penicilline, können den enterohepatischen Kreislauf der weiblichen Sexualhormone, v.a. niedrig dosierter Kontrazeptiva („Mikropille“), unterbrechen und so zu ungewollten Schwangerschaften führen<sup>23</sup>.



### 2.1.3 Physikalische und chemische Wechselwirkungen

Durch Adsorption können manche Arzneimittel andere Wirkstoffe binden und so deren Resorption beeinflussen; ein Beispiel sind Antazida (2- oder 3-wertige Metallsalze), die mit Tetracyclinen schlecht resorbierbare Komplexe bilden<sup>24</sup>.

## 2.2 Elimination und Metabolismus von Arzneimitteln

Wird ein Arzneimittel dem Organismus zugeführt, so durchläuft es mehrere Phasen:

- a) **Pharmazeutische Phase** (Zerfall der Arzneiform und Auflösung der Wirkstoffe nach der Applikation des Arzneimittels)
- b) **Pharmakokinetische Phase** (mit den Teilprozessen Resorption, Verteilung, Elimination)
- c) **Pharmakodynamische Phase** (klinische und toxische Wirkung)

Unter Elimination versteht man den nicht umkehrbaren Verlust der Wirksubstanz aus dem Plasma<sup>25</sup>. Dies erfolgt entweder durch Exkretion (Ausscheidung, hauptsächlich renal) oder durch Metabolisierung (Verstoffwechselung<sup>26</sup>, hauptsächlich hepatisch).

Lipophile Substanzen werden renal nur sehr langsam ausgeschieden, da sie überwiegend rückresorbiert werden<sup>27</sup>. Werden diese Substanzen chemisch nicht verändert, besteht die Gefahr, dass sie sich v.a. im Fettgewebe anreichern.

Die Umwandlung von Fremdstoffen in Substanzen, die vom Organismus schnell wieder ausgeschieden werden können (Biotransformation), dient dem Zweck, eine Anreicherung im Körper zu vermeiden. Ein Beispiel ist die Umwandlung von Ammoniak (das in größeren

Mengen toxisch wirkt) in Harnstoff, eine ungiftige und wasserlösliche Substanz, die über den Urin ausgeschieden wird.

Die Biotransformation lipophiler Xenobiotika (Xenobiotika sind Fremdstoffe, z.Bsp. Medikamente oder Umweltsubstanzen wie Zigarettenrauch) in leichter ausscheidbare hydrophile Substanzen erfolgt im Organismus durch Enzymsysteme, die vor allem in der Leber lokalisiert sind. Es gibt strukturgebundene Enzyme (die vor allem in den Membranen des endoplasmatischen Retikulums vorkommen, ein Beispiel sind Monooxygenasen) und strukturungebundene, lösliche Enzyme, die weniger substratspezifisch sind (zum Beispiel Esterasen).

### 2.2.1 Phase I-Reaktionen

Dazu gehören Biotransformationen, die ein Pharmakonmolekül durch Oxidation, Reduktion, Hydrolyse oder Decarboxylierung verändern. Oft ist die Phase I-Reaktion die Voraussetzung für eine Phase II-Reaktion.

#### 2.2.1.1 Oxidation

Oxidationsreaktionen (eine Reaktion, bei der ein zu oxidierender Stoff Elektronen abgibt) durch **Oxidasen** (Enzyme, die durch Entzug von Wasserstoff bzw. Elektronen oxidieren), **Monooxygenasen** (Enzyme, die ein Sauerstoffatom in den Fremdstoff „einbauen“ und das andere Sauerstoffatom zu Wasser reduzieren) und **Dioxygenasen** (Enzyme, die beide Sauerstoffatome in den Fremdstoff „einbauen“) sind für die Biotransformation von Bedeutung. Die wichtigsten Monooxygenasen für die Biotransformation durch Oxidation sind diejenigen, die Hämproteine vom Typ Cytochrom P450 (CYP) enthalten. Der Name des Enzyms, Cytochrom P450, leitet sich ab von der starken Absorption von Licht der Wellenlänge 450nm, das „P“

steht für Pigment. Die P450-Enzyme sind vielfältig; im menschlichen Körper wurden bislang 18 Enzym-Genfamilien entdeckt, die 57 einzelne CYP-Gene kodieren<sup>28</sup>. Die Enzyme sind nach der Nomenklatur folgendermaßen geordnet: die unterschiedlichen Familien werden als arabische Zahl dargestellt, Subfamilien werden durch einen Buchstaben gekennzeichnet und einzelne Familienmitglieder wiederum mit einer Zahl. Die Familien 1 bis 3 sind für die Metabolisierung von Xenobiotika von größter Bedeutung<sup>29</sup>. Ein Beispiel ist das CYP3A4-Enzym, welches im menschlichen Organismus die stark lipophilen Substanzen oxidiert<sup>30</sup>: es ist ein Cytochrom P-Enzym, das zu der Familie 3 und Subfamilie A gehört und als Subfamilienmitglied 4 definiert ist. Etwa 50% der verordneten Pharmaka werden zumindest teilweise durch CYP3A4 verstoffwechselt<sup>31</sup>.

Das Enzym CYP2D6 erfüllt eine wichtige Funktion bei der Metabolisierung von Xenobiotika. Es ist das am ausführlichsten untersuchte CYP-Enzym. Die ermittelten Polymorphismen sind sehr vielfältig und führen zu unterschiedlichen Ausprägungen in der Enzymaktivität:

- a) **Extensive Metabolisierer** (extensive metabolizers):  
normale Aktivität des Enzyms
- b) **Intermediäre Metabolisierer** (intermediat metabolizers):  
reduzierte Aktivität des Enzyms
- c) **Schlechte Metabolisierer** (poor metabolizers):  
keine Aktivität des Enzyms
- d) **Ultraschnelle Metabolisierer** (ultra extensive metabolizers):  
sehr hohe Aktivität des Enzyms<sup>32</sup>, da gleichzeitig mehrere Kopien des Enzyms  
gebildet wurden

Die Menge an einzelnen P450-Enzymen ist von Mensch zu Mensch sehr unterschiedlich, es bestehen Unterschiede von bis zu 50facher Menge<sup>33</sup>, was auf genetische Polymorphismen<sup>34</sup>,

das Lebensalter des Patienten, das Geschlecht, den Gesundheitszustand und Umwelteinflüsse wie Nikotin oder Chemikalien zurückzuführen ist<sup>35</sup>.

CYP-Enzyme, die ubiquitär (d.h. allgegenwärtig) in fast allen Organismen vorkommen, befinden sich beim Menschen zum größten Teil in der Leber, in geringerer Menge aber auch in vielen anderen Organen wie Gastrointestinaltrakt, Lunge oder Gehirn.

#### **2.2.1.2 Reduktion**

Reduktionsreaktionen beinhalten die Übertragung von Elektronen auf ein Molekül.

Sie spielen im Vergleich zu der Oxidation eine untergeordnete Rolle bei der Biotransformation. Carbonylverbindungen zum Beispiel können durch die Alkoholdehydrogenase zu Alkoholen reduziert werden. Toxikologisch erwähnenswert ist u.a. die reduktive Dehalogenisierung von dem Narkotikum Halothan.

#### **2.2.1.3 Hydrolyse**

Unter Hydrolyse versteht man die Spaltung einer chemischen Verbindung durch die Reaktion mit Wasser, auf diese Weise werden viele Biomoleküle im Stoffwechsel durch Enzyme in ihre Bausteine zerlegt. Zu diesen Enzymen zählen z.Bsp. Esterasen, sie katalysieren die Hydrolyse von Estern in Säuren und Alkohol.

#### **2.2.1.4 Decarboxylierung**

Decarboxylierung ist die Abspaltung eines Kohlenstoffdioxidmoleküls aus einem Molekül, ein Beispiel ist der Abbau der Aminosäure Histidin zu dem biogenen Amin Histamin, einem Gewebshormon.

### **2.2.2 Phase II-Reaktionen**

Die Phase II-Reaktion ist eine Kopplungsreaktion (Konjugation), das bedeutet, dass eine Substanz, die bei einer Phase I-Reaktion entstanden ist, mit einer körpereigenen Substanz gekoppelt wird. Dies geschieht unter Beteiligung meist spezifischer Transferasen (Transferasen sind Enzyme, die die Übertragung einer funktionellen Gruppe, z.Bsp. einer Methylgruppe, von einem Molekül zu einem anderen Molekül katalysieren).

Man kann die Phase II-Reaktionen einteilen in die, bei denen die Kopplung mit einer energiereichen körpereigenen Substanz erfolgt und in die, bei denen die Kopplung nach Aktivierung des Fremdstoffs mit einer nicht aktivierten körpereigenen Verbindung erfolgt.

#### **2.2.2.1 Konjugation mit aktivierter Glucuronsäure**

Mit aktivierter Glucuronsäure werden Phenole, Carbonsäuren und Amine konjugiert und sekundäre und tertiäre Alkohole, die nicht rasch oxidiert werden können.

Glucuronsäure wird durch membrangebundene Glucuronosyltransferasen (UGTs) in aktivierter Form übertragen. UGTs werden unterteilt in zwei Familien (UGT1, UGT2) mit insgesamt 19 Enzymen. Sie kommen vor allem in der Leber vor, aber auch in der Niere und im Darm. Ebenso wie bei den CYP-Enzymen der Monooxygenasen gibt es bei den UGTs Unterschiede in der Substratspezifität<sup>36</sup>; so sind die Substrate des UGT1-A1 pharmakologisch unterschiedlich wirksame Substanzen wie beispielsweise das Zytostatikum Etoposid oder das Kontrazeptivum Ethinylestradiol. Das UGT2-B7 dagegen hat als Substrate zum Beispiel das Opiat Codein und das Antirheumatikum Ibuprofen<sup>37</sup>. Desweiteren unterscheiden sich die UGTs hinsichtlich ihres Expressionsortes, z.Bsp. Gastrointestinaltrakt, Ösophagus, Mammæ und Prostata<sup>38</sup>.

Die Aktivität der einzelnen Enzyme unterliegt einer interindividuellen Variabilität, so ergibt sich z.Bsp. folgende Abstufung: UGT1-A1 > 1-A6 > 2-B15 > 1-A4 = 1-A9 > 2-B7<sup>39</sup>.

Durch die Glucuronisierung von strukturell sehr unterschiedlichen Arzneistoffen (z.Bsp. tri-zyklische Antidepressiva oder nichtsteroidale Antirheumatika) und endogenen Substraten (z.Bsp. Bilirubin, ein Abbauprodukt des Hämoglobins) leisten die UGTs einen wesentlichen Beitrag zur Elimination.

#### **2.2.2.2 Konjugation mit Schwefelsäure (Dihydrogensulfat)**

Durch Sulfatierung werden vor allem Phenole konjugiert. Sie bilden Konjugate mit aktiviertem Sulfat, das durch zytosolische Sulfotransferasen (SULTs) übertragen wird (das Zytosol ist die Flüssigkeit im Zellinneren, sie enthält Wasser, darin gelöste Ionen und Moleküle).

#### **2.2.2.3 Konjugation mit Glycin**

Nicht weiter oxidativ abbaubare Carbonsäuren können Konjugate mit Glycin bilden, zum Beispiel bildet die Benzoesäure mit Glycin das Konjugat Hippursäure, das vom Körper ausgeschieden wird.

#### **2.2.2.4 Bildung von Mercaptursäure-Derivaten**

Diese Konjugationsreaktionen sind mehrstufig, d.h. zunächst werden Glutathion-Konjugate gebildet, katalysiert durch die Glutathion-S-Transferase (GST). (Die GSTs bestehen aus 20 Isoenzymen, unterteilt in zwei Subfamilien: mikrosomale und zytosolische GSTs. Für den Arzneistoffwechsel sind die zytosolischen GSTs von Bedeutung). Von den Glutathion-Konjugaten werden dann zwei Aminosäuren abgespalten und durch N-Acetylierung von

Cystein entsteht schließlich das Endprodukt Mercaptursäure. Die Konjugation mit Glutathion ist ein bedeutsamer Eliminationsweg für elektrophile Verbindungen.

Ein klinisches Beispiel ist die Paracetamol-Intoxikation: ist bei einer Paracetamol-Überdosis die Leber nicht mehr dazu in der Lage, die Hauptmetabolite Glucuronid und Sulfat durch Bio-transformation zu eliminieren, so entstehen toxische Metabolite, v.a. N-Acetylchinonimin. Dieses wird bei lebergesunden Patienten zunächst noch durch Glutathion zu ungiftigen Konjugaten „abgefangen“. Sind die Glutathion-Speicher jedoch erschöpft, kommt es u.U. zu tödlichen Leberzellnekrosen. Ein Antidot (Gegenmittel) ist Acetylcystein, das dem Körper Cystein zum Aufbau von Glutathion zur Verfügung stellt<sup>40</sup>.

#### **2.2.2.5 Acetylierung**

Acetylierung ist die Anlagerung einer Acetyl-Gruppe durch den Austausch mit Wasserstoffatomen.

Durch zytosolische N-Acetyltransferasen (NATs) werden oxidativ nicht abbaubare Substanzen mit Aminogruppen acetyliert. Ein Beispiel ist Isoniazid, ein Antituberkulotikum, das in der Leber zu bis zu 75% acetyliert wird<sup>41</sup>. Bei den N-Acetyltransferasen gibt es zwei Isoenzyme: die ubiquitäre NAT1 und die auf Leber und Gastrointestinaltrakt beschränkte NAT2. Die NAT2 unterliegt genetischen Polymorphismen, diese unterteilen die Patienten in schnelle und langsame Acetylierer<sup>42</sup>.

### 2.2.2.6 Methylierung

Methylierung ist der Transfer von Methylgruppen von einem Molekül zum anderen.

Sie ist eher selten bei den Biotransformationen. Es gibt zum Einen die N-Methylierung (z.Bsp. wird Nicotinamid zu N-Methylnicotinamid umgewandelt, das aktiv ausgeschieden werden kann) und zum Anderen die S-Methylierung durch zwei verschiedene Transferasen: die membranständige Thiolumethyltransferase (TMT), deren Substrat z.Bsp. der ACE-Hemmer Captopril ist, und die, in gelöster Form im Zytoplasma vorhandene, Thiopurin-S-Methyltransferase (TPMT), deren Substrat z.Bsp. das Immunsuppressivum Azathioprin ist.

## 2.3 P-Glykoprotein (P-gp)

Beim Transport von Substanzen durch Membranen bedienen sich die Zellen unterschiedlicher Techniken<sup>43</sup>:

- a) **Diffusion:** Passiver Transport einer Substanz vom Ort höherer Konzentration zum Ort geringerer Konzentration (Konzentrationsgradient) durch die Membran
- b) **Carrier-vermittelter Transport:** Diffusion von polaren Substanzen über bestimmte Transporter und Kanäle
- c) **Aktiver Transport:** Transport gegen einen Konzentrationsgradienten, entweder durch Vesikelbildung (rezeptorvermittelte Endozytose), als primär aktiver Transport mit der ATPase (Adenosintriphosphatase) oder als sekundär aktiver Transport (an einen passiven Transport gekoppelt)



- d) **Pinozytose:** Aufnahme von Flüssigkeiten und darin gelösten Stoffen in die Zelle mittels Vesikeln
- e) **Phagozytose:** Aufnahme fester Stoffe in die Zelle mittels Vesikeln
- f) **Persorption:** mechanischer Durchtritt von unlöslichen Partikeln zwischen den Epithelzellen hindurch

Beim **aktiven Transport** ist der vektorielle Transport (gerichteter Transport von Substanzen durch zelluläre Barrieren hindurch) von großer Bedeutung. Die entsprechenden Transportproteine werden in SLC-Transporter (Solute-Carrier-Familie, etwa 350 verschiedene Proteine, in 47 Familien unterteilt) und in ABC-Transporter (zu ihnen zählt auch das P-Glykoprotein, als gemeinsames Strukturelement besitzen diese Proteine eine **ATP-Binding Cassette**) eingeteilt.

ABC-Transporter gewinnen die Energie für den Transport der Substrate gegen einen Konzentrationsgradienten aus der Hydrolyse von ATP<sup>44</sup> (Adenosintriphosphat). Es wurden bislang 51 Transportproteine gefunden, die man in sieben Familien einteilt (ABCA bis ABCG).

Das P-Glykoprotein wurde als ABCB1 eingeteilt und ist ein sehr gut untersuchter Vertreter der ABC-Transporter (über 13.000 wissenschaftliche Arbeiten bei Pubmed, einer Online-Datenbank für fachspezifische Literatur).

An Krebs erkrankte Patienten unterziehen sich neben einer Operation zur Tumorentfernung und/oder einer Strahlentherapie zur Unterdrückung des Zellwachstums auch oft einer Chemotherapie mit Zytostatika (zellwachstumshemmende Medikamente). Immer wieder wurde festgestellt, dass ein anfänglich gutes Ansprechen auf eine Chemotherapie nach wenigen Monaten in einem schweren Rezidiv resultierte. Wurde erneut eine Chemotherapie angesetzt, reagierten die Tumorzellen nicht mehr auf die beim ersten Mal eingesetzten Zytostatika. Der

Grad an Resistenz gegen Zytostatika variierte von Patient zu Patient und stellte die Ärzte vor ein Rätsel, dass 1976 mit der Entdeckung des P-Glykoproteins teilweise gelöst werden konnte.

Erstmals beschrieben wurde es bei einem Tierversuch (Studie über Hamster-Ovarzellen, die eine Resistenz gegen das Alkaloid Colchizin und andere Medikamente aufweisen), die Wissenschaftler nannten ihre Entdeckung P-Glykoprotein. Hierbei steht „P“ für Permeabilität, da das Protein die Permeabilität der Zelle gegenüber Medikamenten verändert, und „Glykoprotein“ bezieht sich auf eine Kohlenhydratkomponente, die das entdeckte Protein aufweist. Das P-gp ist ein membranständiges Protein mit einem Molekulargewicht von 170kD<sup>45</sup>.

Etwa sieben Jahre später konnte in einer vergleichenden Studie über chemotherapieresistente tierische und menschliche Tumorzellen<sup>46</sup> das Vorhandensein von Pgp im menschlichen Körper nachgewiesen werden.

Das P-gp ist annähernd 1280 Aminosäuren lang und besteht aus zwei homologen Teilen, die etwa gleich groß sind. Beide Hälften enthalten eine hydrophobe Region mit sechs transmembranären Segmenten und eine hydrophile Region<sup>47</sup>.

Jede Hälfte enthält eine Bindestelle für ATP, durch dessen Spaltung das Protein die Energie für den extrazellulären Transport von Substraten gewinnt<sup>48</sup>.

Das Protein ist in der Lage, eine breitgefächerte Reihe von Substraten aus der Zelle zu befördern; Arzneistoffe, Nahrungsbestandteile, Umweltgifte, Hormone, Aminosäuren, Zucker und Peptide, d.h., Moleküle von 400 bis circa 2000Da werden transportiert<sup>49</sup>.

Das P-Glykoprotein ist das Produkt eines Gens, das 1985 bei menschlichen Zellen entdeckt wurde, die resistent gegen Zytostatika waren<sup>50</sup>.

Genannt wurde das Gen MDR-Gen, MDR steht hierbei für Multi Drug Resistance (Vielfach-Resistenz). Multi Drug Resistance bedeutet, dass die Zellen gegen eine Vielzahl strukturell und funktionell unterschiedlicher Verbindungen resistent sind.

Es sind zwei verschiedene MDR-Gene bekannt: das MDR1-Gen, das viele verschiedene Substanzen aus der Zelle hinaus transportiert, und das homologe MDR3-Gen, das ausschließlich Phosphatidylcholin transportiert<sup>51</sup>. Die Menge an MDR1-Gen hat eine direkte Auswirkung auf die Resistenz einer Zelle, denn je mehr MDR1-Gen eine Zelllinie enthält, desto resistenter gegen Zytostatika ist sie<sup>52</sup>.

Als Genort des MDR1-Gens wurde der lange Arm des Chromosoms 7 der menschlichen DNA entdeckt<sup>53</sup>.

Das MDR1-Gen tritt vielgestaltig auf, mindestens 15 Polymorphismen an einzelnen Nukleotiden (Grundbausteine der DNA) wurden identifiziert, was weitreichende Folgen für die Expression von P-gp beim Individuum hat (Expression = Umsetzung der genetischen Information): z.Bsp. beeinflusst ein Polymorphismus an Position 3435 im Exon 26 die Menge an intestinalem P-gp, was bei 61% der Afro-Amerikaner und 26% der kaukasischen Amerikaner zu deutlich weniger intestinalem P-gp führt<sup>54</sup>.

Das P-gp besitzt eine **Clearancefunktion** (Entfernung von Substanzen aus einem Körpersystem), weil es in der Lage ist, die Absorption von Xenobiotika zu kontrollieren und diese Stoffe wieder in den Darm, die Galle oder den Urin abzugeben. P-gp kommt in der Leber in den apikalen Hepatozyten vor, die an die Gallenkapillare angrenzen. Desweiteren tritt P-gp in der Niere an den apikalen Oberflächen von Epithelzellen der proximalen Tubuli auf, ebenso in Kolon und Jejunum an den apikalen Oberflächen von Zylinderepithelzellen. In der Nebenniere wurde an der Oberfläche von Zellen in Rinde und Mark erhöhte Konzentrationen an P-gp gefunden<sup>55</sup>.

Das P-gp erfüllt auch eine **Barrierefunktion**, da es Substanzen, die die Blut-Hirn-Schranke überquert haben, wieder in den Intravasalraum zurücktransportiert und so das Gehirn vor Fremdstoffen schützt<sup>56</sup>.

Die Therapieresistenz, die bei vielen Patienten auftritt, entsteht durch diese Funktionen des P-gp: die Medikamente erreichen ihren Wirkort nicht, weil sie vom „Wächter“ P-gp aus den Zellen transportiert werden.

Das Stoffwechselenzym Cytochrom P450-3A4 teilt sich oft Zellen und Substrate mit dem P-gp, wodurch man von einem kombinierten Mechanismus ausgeht: Erst wird ein Substrat von dem Cytochrom P450-Enzym verstoffwechselt und dann von P-gp durch die Zellmembran nach außen geschleust<sup>57</sup>.

## 2.4 Pharmakovigilanzsysteme

Unter Pharmakovigilanz versteht man die Überwachung von Arzneimitteln, besonders nach deren Marktzulassung<sup>58</sup>. Diese sogenannten Phase IV-Studien leisten einen wichtigen Beitrag zur Aufdeckung von unerwünschten Arzneimittelwirkungen (UAW). In den vorausgehenden klinischen Studien ist es nicht vollständig möglich, seltene und sehr seltene UAW zu erkennen und WW im Zusammenhang mit der Arzneimittelanwendung zu beurteilen.

Die Entwicklung und Markteinführung eines neuen Arzneimittels ist in mehrere Phasen unterteilt<sup>59</sup>:

**Präklinische Studien:** Im Labor, an Zell- und Tiermodellen werden neue Arzneistoffe entdeckt und geprüft und daraufhin die Zulassung zur Phase I-Studie beantragt.

**Phase I:** Bei ca. 30-100 gesunden Probanden werden Pharmakokinetik, Pharmakodynamik und Verträglichkeit einer Substanz getestet.

**Phase II:** Ca. 100-3000 Patienten erhalten den Arzneistoff, Ziel ist die Ermittlung der richtigen Dosis.

**Phase III:** Bei ca. 3000-15.000 Patienten werden Nebenwirkungen und Wirksamkeit dokumentiert.

**Phase IV:** Bereits auf dem Markt eingeführte Arzneimittel werden systematisch überwacht.

Die WHO definierte Pharmakovigilanz 2002 als die Wissenschaft und die Aktivitäten, die im Zusammenhang mit der Entdeckung, der Bewertung, dem Verständnis und der Prävention von Nebenwirkungen oder anderen Problemen stehen, die mit der Arzneimittelgabe zusammenhängen. Dabei bedeutet Pharmakovigilanz dasselbe wie „Drug Monitoring“.

Im Jahr 2000 gab die WHO in ihren Leitlinien bekannt, dass zu den Funktionen der Pharmakovigilanz folgende Punkte gehören:

- Entdeckung und Studium der Nebenwirkungen
- Risikobewertung
- Effektivitätsbewertung
- Risiko-Nutzen-Abwägung
- Weitergabe von Informationen, Bildung<sup>60</sup>

Pharmakovigilanzsysteme sind von unterschiedlicher Art:

- a) **Spontanmeldesysteme:** Die Arzneimittelkommissionen der Heilberufskammern haben seit 1978 in der Bundesrepublik den Auftrag, von Ärzten, Zahnärzten, Tierärzten und Apothekern Meldungen über aufgetretene UAW zu sammeln.
- b) **Intensivierte UAW-Erfassung:** Die UAW einer begrenzten Population werden über einen bestimmten Zeitraum erfasst.

- c) **Prescription-Event-Monitoring (PEM):** Bei den ersten 10 000 Patienten werden die UAW eines neu auf dem Markt erhältlichen Medikaments erfasst, ein System, das z.Bsp. in Großbritannien angewendet wird.
- d) **Nationale Pharmakovigilanzzentren:** Ergänzend zum Spontanmeldesystem werden hierbei UAW bei Krankenhausaufnahmen, schweren Krankheitsbildern und spezifischen Patientengruppen erfasst.
- e) **Kontrollierte Studien:** Groß angelegte Studien ergeben repräsentative Meldungen über UAW bezogen auf den Bevölkerungsquerschnitt.

In Bayern wird die Erfassung und Dokumentation schwerer UAW bei Psychopharmaka unter anderem durch AGATE koordiniert, die Arbeitsgemeinschaft “Arzneimitteltherapie bei psychiatrischen Erkrankungen”, die sich aus der seit 1979 bestehenden AMÜP-Bayern weiterentwickelte (Arzneimittelüberwachung in der Psychiatrie Bayern). Derzeit nehmen ca. 40 Kliniken am umfangreichen Programm der AGATE teil, wozu auch Nutzen-Risiko-Bewertung neuer Wirkstoffe, Schwangerschaftsberatung und klinische Studien in einem Klinikverbund mit 10.000 Betten gehören. Dieses effektive Pharmakovigilanzsystem der AGATE trägt seit dem Jahr 2000 maßgeblich zur Vermeidung von UAW bei<sup>61</sup>.

## 2.5 Therapeutisches Drug Monitoring (TDM) in der Psychiatrie

Nur etwa 40-60% der Patienten, denen Antidepressiva, Neuroleptika oder Antiepileptika verschrieben werden, sprechen auf die Arzneimittel in therapeutisch erforderlicher Weise an; dies belegt auch eine aktuelle Studie über die Behandlung von MDD (Major Depressive Disorder) mit Antidepressiva bei 101 Patienten: 35 sprachen schnell auf die Medikamente an, 66 jedoch überhaupt nicht<sup>62</sup>.

Oft treten UAW auf oder es fehlt eine therapeutische Wirkung nach Gabe des Medikaments. Diese Phänomene führt man darauf zurück, dass es interindividuell Unterschiede bei der Pharmakokinetik und Pharmakodynamik gibt, dies führt zu stark variierenden Plasmakonzentrationen bei den Patienten.

Beim TDM wird die Plasmakonzentration einer Substanz gemessen und hierbei auch die Dosis, die Komedikation und der Zeitpunkt der letzten Applikation berücksichtigt. Anschließend wird die Dosis individuell angepasst<sup>63</sup>. Besonders sinnvoll ist das TDM bei bestimmten Pharmaka, bei denen aufgrund einer geringen therapeutischen Breite ein relativ hohes Intoxikationsrisiko besteht<sup>64</sup>. Zum Beispiel ist bei Lithiumsalzen (Stimmungsmodulatoren) eine wiederholte Kontrolle der Plasmakonzentration erforderlich, um solch eine Intoxikation zu vermeiden. Durch die geringe therapeutische Breite der Lithiumsalze ist jedoch auch bei genauer Einstellung des Lithiumspiegels mit Nebenwirkungen zu Therapiebeginn zu rechnen<sup>65</sup>.

### 3 Material und Methoden

Die Grundlage war eine Recherche bei Pubmed, einer Datenbank für fachspezifische Literatur im Internet. Sie enthält über 19 Millionen Literaturstellen von biomedizinischen Studien und biowissenschaftlichen Fachzeitschriften und verweist bei jeder Literaturstelle durch einen angefügten Link auf den Volltext der Forschungsarbeit.

Das Ziel war, alle in der Wissenschaft veröffentlichten Artikel über Wechselwirkungen zwischen P-Glykoprotein und einem Medikament aus einer Liste zu finden, die 2007 als Cytochrom P450-Interaktionstabelle unter der Leitung von Prof. Dr. Haen erarbeitet wurde. Die Liste enthält in alphabetischer Ordnung 504 Substanzen, die zum größten Teil pharmakologische Substanzen im Sinne von chemisch hergestellten Medikamenten sind. Es befinden sich aber auch Substanzen wie das natürliche Östrogen Estradiol oder der Alkohol Ethanol auf der Liste, ebenso sind auch körpereigene Substanzen vertreten wie z.Bsp. das in der Bauchspeicheldrüse produzierte Peptidhormon Insulin. In der ersten Spalte der Interaktionstabelle sind die Arzneimittel aufgeführt. Beschäftigen sich relevante Artikel mit Derivaten oder Metaboliten dieser Arzneimittel, so sind diese hellgrau unterlegt und direkt unter der Ausgangssubstanz aufgeführt, so zum Beispiel **Diacetolol**, ein Metabolit von Acebutolol.

Die Literatursuche für die Interaktionstabelle ist auf dem Stand von September 2009, sodass nach diesem Zeitpunkt veröffentlichte Artikel in der Tabelle keine Erwähnung finden.

Die einzelnen Substanzen der Liste wurden in der Wissenschaftssprache Englisch bei <http://www.pubmed.com> eingegeben. Die angezeigten Treffer waren im bis zu fünfstelligen Bereich und zeigten auf, dass die gesuchten Artikel nur mit genaueren Angaben zu finden waren.

Daher beschränkte ich die Suche auf den Namen aus der Liste, z.Bsp. das Medikament „verapamil“ und fügte das von mir untersuchte Protein „p-glycoprotein“ hinzu, verbunden mit einem „and“. Es machte hierbei keinen Unterschied, ob das „and“ eingefügt oder weggelassen



wurde. Unter der Abkürzung „p-gp“ für das P-Glykoprotein fand Pubmed weniger Artikel, daher wurde der Proteinname ausgeschrieben. Durch den Verbund von Substanz und Protein lieferte die Suchmaschine Pubmed diejenigen Artikel, die sich mit der Substanz auseinandersetzten und gleichzeitig in Zusammenhang mit P-Glykoprotein standen.

Die Ergebnisse befanden sich nun je nach Substanz im bis zu vierstelligen Bereich, was immer noch eine unübersichtliche Menge an Artikeln darstellte und daher weiter eingeschränkt werden musste. Dies geschah über eine Feineinstellung bei der Artikelsuche, die sogenannten „limits“. Hier ist es unter anderem möglich, Studien suchen zu lassen, die in einem vorher festgelegten Zeitraum veröffentlicht wurden oder die ein bestimmtes Studiendesign aufweisen (z.Bsp. nur klinische Studien: „clinical trials“, oder nur Übersichtsartikel der aktuellen Forschungslage: „reviews“).

Im Fall des Medikaments Verapamil ergaben sich ohne „limits“ 2134 Artikel, die die Schlagwörter „verapamil and p-glycoprotein“ aufwiesen. Als erste Limitierung wurde „reviews“ eingeschaltet, was die Zahl der relevanten Artikel auf 125 einschränkte, die eine gute Übersicht über die Studienlage bei dieser Substanz lieferten. Da die Studien aber bis zum Jahr 1987 zurückreichen und ich die Tabelle auf einem möglichst zeitnahen Wissenschaftsstand halten wollte, wurde als weitere Feineinstellung das Suchergebnis auf die aktuellen Forschungsergebnisse der letzten fünf Jahre beschränkt: „5 years“.

Bei Verapamil lieferte das ein zu verwertendes Ergebnis der 23 aktuellsten Übersichtsartikel. Beim Sichten der Artikel zeigte sich, dass Verapamil ein **Inhibitor** des Proteins ist, daher sind die betreffenden Artikel in der Spalte „Substrat/Inhibitor/Induktor“ **rot** unterlegt (**grün** unterlegte Treffer stehen für **Induktoren**, unmarkierte Treffer für Substrate). Einige Artikel berichten von der Umkehr einer Multi Drug Resistance durch Verapamil, sie sind in der „MDR-Umkehr“-Spalte aufgeführt.

In der Spalte „Wechselwirkungen“ sind die Studien erfasst, die eine Interaktion zwischen Verapamil und einer anderen Substanz nachweisen (z.Bsp. Rifampin), von der die Interaktion

ausgeht. Hat umgekehrt Verapamil eine Wirkung auf eine andere Substanz, so steht dies bei der anderen Substanz in der Wechselwirkungen-Spalte, wie es z.Bsp. bei Methylprednisolon der Fall ist.

Die in der Tabelle vermerkten Wechselwirkungen treten unter Beteiligung des P-Glykoproteins auf. Die wissenschaftlichen Studien, in denen nicht nachgewiesen wurde, ob die Wechselwirkung über das P-Glykoprotein oder das CYP-Enzym zustande kommt, sind in der Tabelle mit einem grau unterlegten „cop“ (Cyp-Enzym oder P-Glykoprotein) vermerkt.

Lieferten die Feineinstellungen „reviews“ und „5 years“ nicht das gewünschte Ergebnis, z.Bsp. aufgrund zu weniger Artikel für eine repräsentative Darstellung der Wissenschaftslage, so wurde eine andere Feineinstellung angewandt, das „limit“ „humans“. Hier wurde nach Artikeln gesucht, die sich ausschließlich mit menschlichen Zellen oder Versuchspersonen bzw. Patienten beschäftigten. Dieses „limit“ reduzierte z.Bsp. bei der Substanz Saquinavir gemeinsam mit „5 years“ die anfängliche Trefferzahl von 102 Artikeln auf die 37 aktuellsten und für die Patienten relevantesten Artikel. Eine Studie über Saquinavir ergab, dass die Substanz eine induzierende Wirkung auf die Expression von P-gp hat, was grün unterlegt mit der Abkürzung „Pgp“ in einer eigenen Spalte angeführt ist : „Wirkung auf die Funktion von...“/ „Wirkung auf die Expression von...“. Die Spalten über die Beeinflussung der „Expression“ und „Funktion“ von P-gp und verwandten Transportenzymen wurden eingerichtet, da einige Studien diesen wichtigen Sachverhalt beleuchteten, ohne dabei aber auf die Substanz als evtl. Substrat, Induktor oder Inhibitor einzugehen.

Rofecoxib z.Bsp. hat sowohl auf die Funktion, als auch auf die Expression von P-gp eine inhibierende Wirkung und ist daher rot unterlegt.

Doxorubicin ist ein Beispiel für ein bereits seit dem Jahr 1983 sehr gut erforschtes Arzneimittel, die Literatursuche auf Pubmed ergab 2186 Treffer. Stellvertretend für eine grosse Anzahl ähnlicher Studienergebnisse habe ich in der Tabelle drei repräsentative Artikel aufgeführt.

Weitere Spalten wurden hinzugefügt, um dem Bedarf nach detaillierterer Aufteilung nachzukommen. So ist z.Bsp. das Medikament Nelfinavir einerseits Substrat und Inhibitor der Multidrug-Resistance-related-Proteine MRP1 und MRP2, andererseits ergaben Studien, dass Nelfinavir auch ein Inhibitor des Breast-Cancer-Resistance-Proteins BCRP1 und ein Substrat und Inhibitor des P-Glykoproteins ist. Die Tabelle enthält aufgrund der Suchergebnisse die Transportenzyme MRP1, MRP2, MRP3 und MRP4. Beim Menschen sind neun dieser Transportmembranproteine bekannt (MRP1 bis MRP9), die zur Familie ABCC der ABC-Transporter gehören. BCRP1 wird der Familie ABCG2 der ABC-Transportproteine zugeteilt.

Eine Spalte mit der Bezeichnung „Zusatz“ wurde eingerichtet, um kontroverse oder nicht tabellenkompatible Studienergebnisse festzuhalten. Zum Beispiel lieferte das Medikament Quetiapin in drei Studien das Ergebnis „Substrat von P-gp“, in einer Studie „Inhibitor von P-gp“ und in einer Studie „kein Substrat von P-gp“; diese gegensätzlichen Ergebnisse sind in der Spalte „Zusatz“ vermerkt. Ein weiteres Beispiel ist die Substanz Digitoxin, die einerseits als „Substrat von P-gp“ aus der Literatursuche hervorgeht, in einer Studie aber auch als „Modulator“ bezeichnet wird. Da in dem Artikel nicht geklärt wurde, ob diese Modulation durch Induktion oder Inhibition erfolgt, habe ich den betreffenden Artikel mit dem Schlagwort „Modulator“ in der Spalte „Zusatz“ abgelegt.

Ebenso erschienen mir Studien relevant, in denen ein qualitatives oder quantitatives Ergebnis veröffentlicht wurde; so ist z.Bsp. Bupropion ein „Substrat von P-Glykoprotein“. In der Studie wird aber angegeben, dass es sich um ein sehr schwaches Substrat handelt, dies ist in der Spalte „Zusatz“ vermerkt.

Weitere „Sonderergebnisse“ sind in der „Zusatz“-Spalte jeweils mit einer kurzen Bezugnahme auf die Art des Ergebnisses vermerkt; das Derivat Desacetyl-Diltiazem, ein P-gp-Substrat, ist z.Bsp. in der „Zusatz“-Spalte des Medikaments Diltiazem vermerkt.

Die Art der Studie steht abgekürzt in der Tabelle, um die Suche nach spezifischen „Studiendesigns“ zu erleichtern: „vt“ steht für In-vitro-Studien mit Zell-Linien (d.h. das Experiment

wurde in einer kontrollierten künstlichen Umgebung außerhalb eines lebenden Organismus durchgeführt), „r“ für „review“-Artikel (diese Artikel stellen eine Übersicht über die derzeitige Studienlage dar), „t“ für Versuche an Tieren und „h“ für Versuche mit Menschen. Ein Beispiel ist das Medikament Tamoxifen: eine Studie mit Zell-Linien ergab, dass Tamoxifen eine induzierende Wirkung auf die Expression des MDR1-Gens hat, eine „review“-Arbeit beschäftigte sich mit der Multi Drug Resistance-Umkehr durch Tamoxifen, eine Studie an Tieren lieferte das Ergebnis „Inhibitor von P-gp“ und ein Versuch mit Menschen ergab, dass Tamoxifen ein Substrat von P-gp ist. Dem durchmischten Gesamtergebnis liegen die unterschiedlichen Studienbedingungen und -ansätze der Forscher zugrunde.

## 4 Ergebnisse

### 4.1 Interaktionstabelle

| Substanz                    | Anzahl Artikel | Wirkung auf Funktion von                                              | Wirkung auf Expression von                                                                                                            | MDR-Umkehr | MRP 1 | MRP 2   | MRP 3 | MRP 4 | BCRP 1  | Pgp                                    | Zusatz | Wechselwirkungen                     |
|-----------------------------|----------------|-----------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|------------|-------|---------|-------|-------|---------|----------------------------------------|--------|--------------------------------------|
| Acebutolol                  | 6              |                                                                       |                                                                                                                                       |            |       |         |       |       |         | $X_{vt}^1$<br>$X_{vt}^2$<br>$X_{vt}^3$ |        |                                      |
| Diacetolol                  |                |                                                                       |                                                                                                                                       |            |       |         |       |       |         | $X_{vt}^4$                             |        |                                      |
| Acenocoumarol               | 0              |                                                                       |                                                                                                                                       |            |       |         |       |       |         |                                        |        |                                      |
| Acetaminophen (Paracetamol) | 13             | Pgp, Mrp2 <sup>1</sup> <sub>t</sub><br>Pgp <sup>2</sup> <sub>vt</sub> | Pgp, Mrp2 <sup>1</sup> <sub>t</sub><br>Pgp <sup>2</sup> <sub>vt</sub><br>MRP1, MRP4,<br>MRP5, BCRP,<br>Pgp <sup>3</sup> <sub>vt</sub> |            |       |         |       |       |         | $X_{vt}^2$<br>$X_{vt}^4$               |        | Verapamil <sup>2</sup> <sub>vt</sub> |
| Acetaminophen-Sulfat        | 1              |                                                                       |                                                                                                                                       |            |       | $X_t^5$ |       |       | $X_t^1$ |                                        |        |                                      |
| Acetazolamid                | 2              |                                                                       |                                                                                                                                       |            |       |         |       |       |         | $X_{vt}^1$                             |        |                                      |

|                           |    |                                |                                                                    |                                                              |  |  |  |                              |                                                                                            |                                                                                  |  |  |
|---------------------------|----|--------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------|--|--|--|------------------------------|--------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|--|--|
| Acetylsalicyl-<br>säure   | 8  |                                | P-gp <sup>1</sup> <sub>vt</sub><br>P-gp <sup>2</sup> <sub>vt</sub> |                                                              |  |  |  |                              |                                                                                            |                                                                                  |  |  |
| Adrenalin                 | 1  |                                | MDR1 <sup>1</sup> <sub>vt</sub>                                    |                                                              |  |  |  |                              |                                                                                            |                                                                                  |  |  |
| Äthanol                   | 34 | Pgp <sup>1</sup> <sub>t</sub>  | Pgp <sup>1</sup> <sub>t</sub>                                      |                                                              |  |  |  |                              |                                                                                            |                                                                                  |  |  |
| Äthanolextrakt            | 1  |                                |                                                                    |                                                              |  |  |  |                              | X <sup>1</sup> <sub>vt</sub>                                                               | aus dem Rhizom der<br>Kaempferia parviflora                                      |  |  |
| Äthanol-<br>jodiertes Öl  | 1  |                                |                                                                    | X <sup>1</sup> <sub>vt</sub>                                 |  |  |  |                              |                                                                                            | in Kombination mit<br>Chemotherapie und<br>Sga (Spongia gelatini<br>absorbens)   |  |  |
| Cremophor                 | 2  | Pgp <sup>1</sup> <sub>vt</sub> |                                                                    | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> |  |  |  |                              |                                                                                            | 50% Äthanol und 50%<br>polyethoxyliertes Surfac-<br>tant Cremophor EL            |  |  |
| Äthanolamin               | 31 |                                |                                                                    |                                                              |  |  |  |                              | X <sup>1</sup> <sub>vt</sub>                                                               |                                                                                  |  |  |
| Äthinylöstradiol          | 5  |                                |                                                                    |                                                              |  |  |  |                              | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>t</sub><br>X <sup>3</sup> <sub>t</sub> |                                                                                  |  |  |
| Äthylöstradiol            | 0  |                                |                                                                    |                                                              |  |  |  |                              |                                                                                            |                                                                                  |  |  |
| Äthylmorphin              | 0  |                                |                                                                    |                                                              |  |  |  |                              |                                                                                            |                                                                                  |  |  |
| Ätonorgestrel             | 0  |                                |                                                                    |                                                              |  |  |  |                              |                                                                                            |                                                                                  |  |  |
| Ajmalin                   | 2  |                                |                                                                    |                                                              |  |  |  |                              |                                                                                            |                                                                                  |  |  |
| APDA                      |    |                                |                                                                    |                                                              |  |  |  |                              | X <sup>1</sup> <sub>vt</sub>                                                               | Ajmalin nach<br>N-Alkylation:<br>N-(4',4'-azo-in-pentyl)-21-<br>deoxy-ajmalinium |  |  |
| Albendazol                | 7  |                                |                                                                    |                                                              |  |  |  |                              |                                                                                            |                                                                                  |  |  |
| Albendazol-<br>Sulfoxid   |    |                                |                                                                    |                                                              |  |  |  | X <sup>1</sup> <sub>vt</sub> |                                                                                            |                                                                                  |  |  |
| Albuterol<br>(Salbutamol) | 4  |                                |                                                                    |                                                              |  |  |  |                              | X <sup>1</sup> <sub>t</sub>                                                                |                                                                                  |  |  |
| Salbutamol-<br>Sulfat     |    |                                |                                                                    |                                                              |  |  |  |                              | X <sup>1</sup> <sub>t</sub>                                                                |                                                                                  |  |  |
| Aldosteron                | 15 |                                | MDR1-<br>Pgp/MDR1-<br>mRNA <sup>1</sup> <sub>vt</sub>              |                                                              |  |  |  |                              | X <sup>2</sup> <sub>t</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>h</sub> |                                                                                  |  |  |

|                            |    |                                |                                 |  |                              |  |  |  |                              |                                                                                                                                                             |                                                            |                                                      |
|----------------------------|----|--------------------------------|---------------------------------|--|------------------------------|--|--|--|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------|
| Alfentanil                 | 8  |                                |                                 |  |                              |  |  |  |                              | X <sub>t</sub> <sup>1</sup><br>X <sub>vt</sub> <sup>2</sup>                                                                                                 | kein Substrat <sup>3</sup> <sub>h</sub>                    |                                                      |
| Alkohol<br>-siehe Äthanol- |    |                                |                                 |  |                              |  |  |  |                              |                                                                                                                                                             |                                                            |                                                      |
| Almotriptan                | 0  |                                |                                 |  |                              |  |  |  |                              |                                                                                                                                                             |                                                            |                                                      |
| Alprazolam                 | 8  |                                |                                 |  |                              |  |  |  |                              |                                                                                                                                                             |                                                            | Pflanzl. Arzneimittel <sup>1</sup> <sub>r, cop</sub> |
| Alprenolol                 | 2  |                                |                                 |  |                              |  |  |  |                              |                                                                                                                                                             |                                                            |                                                      |
| Aminogluthethimid          | 3  | Pgp <sup>1</sup> <sub>vt</sub> | MDR1 <sup>1</sup> <sub>vt</sub> |  |                              |  |  |  |                              |                                                                                                                                                             |                                                            |                                                      |
| Aminophyllin               | 0  |                                |                                 |  |                              |  |  |  |                              |                                                                                                                                                             |                                                            |                                                      |
| Amiodaron                  | 36 |                                |                                 |  |                              |  |  |  |                              | X <sub>vt</sub> <sup>1</sup><br>X <sub>r</sub> <sup>2</sup><br>X <sub>vt</sub> <sup>3</sup><br>X <sub>vt</sub> <sup>4</sup><br>X <sub>r</sub> <sup>5</sup>  | Substrat/<br>Modulator von ABCR <sup>6</sup> <sub>vt</sub> |                                                      |
| N-Monodesethyl-Amiodaron   | 1  |                                |                                 |  |                              |  |  |  |                              | X <sub>h, vt</sub> <sup>1</sup>                                                                                                                             |                                                            |                                                      |
| Desethyl-Amiodaron         | 1  |                                |                                 |  |                              |  |  |  |                              | X <sub>vt</sub> <sup>2</sup>                                                                                                                                |                                                            |                                                      |
| Amisulprid                 | 3  |                                |                                 |  |                              |  |  |  |                              | X <sub>t</sub> <sup>1</sup> <sub>h, vt,</sub>                                                                                                               |                                                            |                                                      |
| Amitryptilin               | 1  |                                |                                 |  |                              |  |  |  |                              | X <sub>vt</sub> <sup>1</sup>                                                                                                                                |                                                            |                                                      |
| Amlodipin                  | 10 |                                |                                 |  |                              |  |  |  |                              | X <sub>vt</sub> <sup>1</sup>                                                                                                                                |                                                            |                                                      |
| CJX1/2                     |    |                                |                                 |  |                              |  |  |  |                              | X <sub>vt</sub> <sup>1</sup>                                                                                                                                |                                                            |                                                      |
| Amobarbital                | 0  |                                |                                 |  |                              |  |  |  |                              |                                                                                                                                                             |                                                            |                                                      |
| Amphetamin                 | 7  |                                |                                 |  |                              |  |  |  |                              | X <sub>vt</sub> <sup>1</sup>                                                                                                                                | schwacher Inhibitor                                        |                                                      |
| MDMA, MDE, PMA             |    |                                |                                 |  |                              |  |  |  |                              | X <sub>h, vt</sub> <sup>1</sup>                                                                                                                             |                                                            |                                                      |
| Amprenavir                 | 36 |                                | Pgp <sup>1</sup> <sub>r</sub>   |  | X <sub>vt</sub> <sup>2</sup> |  |  |  | X <sub>vt</sub> <sup>3</sup> | X <sub>vt</sub> <sup>2</sup><br>X <sub>vt</sub> <sup>4</sup><br>X <sub>t</sub> <sup>5</sup><br>X <sub>vt</sub> <sup>6</sup><br>X <sub>vt</sub> <sup>7</sup> | kein Substrat <sup>8</sup> <sub>vt</sub>                   | Quinidin <sup>7</sup> <sub>vt</sub>                  |

| Amrinon                  | 0              |                                      |                                                                                                     |                                                              |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |
|--------------------------|----------------|--------------------------------------|-----------------------------------------------------------------------------------------------------|--------------------------------------------------------------|-------|-----------------------------|-------|-------|--------|----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|
| Anastrozol               | 2              |                                      |                                                                                                     |                                                              |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |
| Androsteron              | 1              |                                      |                                                                                                     |                                                              |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |
| Anilin                   | 27             |                                      |                                                                                                     |                                                              |       |                             |       |       |        | X <sup>1</sup> <sub>vt</sub>                                                                 |                                                                                          |                                                                                                                              |
| Aprindin                 | 0              |                                      |                                                                                                     |                                                              |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |
| Aripiprazol              | 0              |                                      |                                                                                                     |                                                              |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |
| Astemizol                | 6              |                                      |                                                                                                     |                                                              |       |                             |       |       |        | X <sup>1</sup> <sub>vt</sub>                                                                 |                                                                                          |                                                                                                                              |
| Atorvastatin             | 29             |                                      | ABCB1 <sup>1</sup> <sub>vt</sub>                                                                    |                                                              |       |                             |       |       |        | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub> |                                                                                          | Colchizin <sup>5</sup> <sub>h</sub><br>Cyclo-<br>sporin A <sup>6</sup> <sub>h</sub><br>Esomeprazol <sup>7</sup> <sub>h</sub> |
| Lakton-/Azid-<br>Form    |                |                                      |                                                                                                     |                                                              |       |                             |       |       |        | X <sup>1</sup> <sub>t</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub>  | schwach <sup>1</sup><br>schwach bis moderat <sup>2</sup><br>nur Lakton-Form <sup>3</sup> |                                                                                                                              |
| Azapropazon              | 0              |                                      |                                                                                                     |                                                              |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |
| Azelastin                | 2              |                                      |                                                                                                     | X <sup>1</sup> <sub>vt</sub>                                 |       |                             |       |       |        | X <sup>2</sup> <sub>vt</sub>                                                                 |                                                                                          |                                                                                                                              |
| Azithromycin             | 16             |                                      |                                                                                                     | X <sup>1</sup> <sub>vt</sub>                                 |       | X <sup>2</sup> <sub>t</sub> |       |       |        | X <sup>3</sup> <sub>t</sub><br>X <sup>4</sup> <sub>vt</sub>                                  |                                                                                          |                                                                                                                              |
| Substanz                 | Anzahl Artikel | Wirkung auf Funktion von             | Wirkung auf Expression von                                                                          | MDR-Umkehr                                                   | MRP 1 | MRP 2                       | MRP 3 | MRP 4 | BCRP 1 | Pgp                                                                                          | Zusatz                                                                                   | Wechselwirkungen                                                                                                             |
| Beclometason             | 3              |                                      |                                                                                                     |                                                              |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |
| Beclometason-Dipropionat |                | Pgp, BCRP <sup>1</sup> <sub>vt</sub> | Pgp, Mrp1, Mrp2 <sup>2</sup> <sub>vt</sub>                                                          |                                                              |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |
| Benzafibrat              | 0              |                                      |                                                                                                     |                                                              |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |
| Bepridil                 | 7              |                                      |                                                                                                     | X <sup>1</sup> <sub>h</sub><br>X <sup>2</sup> <sub>h</sub>   |       |                             |       |       |        | X <sup>3</sup> <sub>vt</sub>                                                                 |                                                                                          |                                                                                                                              |
| Betamethason             | 2              |                                      |                                                                                                     |                                                              |       |                             |       |       |        | X <sup>1</sup> <sub>vt</sub>                                                                 |                                                                                          |                                                                                                                              |
| Betaxolol                | 0              |                                      |                                                                                                     |                                                              |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |
| Bezafibrat               | 5              |                                      | MDR3 <sup>1</sup> <sub>vt</sub><br>mdr2 <sup>2</sup> <sub>t</sub><br>Mrp2 <sup>3</sup> <sub>t</sub> |                                                              |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |
| Bexaroten                | 4              |                                      |                                                                                                     | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> |       |                             |       |       |        |                                                                                              |                                                                                          |                                                                                                                              |



|                        |                           |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
|------------------------|---------------------------|---------------------------------------------------------------------|-----------------------------------------------------------------------------|-----------------------------------------------------------------|--------------------------------------------------------------|------------------------------|------------------|------------------|-------------------|----------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|------------------------------------|
|                        |                           |                                                                     |                                                                             | X <sup>3</sup> <sub>vt</sub>                                    |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
| Biperiden              | 0                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
| Bisoprolol             | 2                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   | X <sup>4</sup> <sub>vt</sub>                                   |                                                                                                       |                                    |
| Bopindolol             | 0                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
| Bosentan               | 3                         | Mrp2 <sup>1</sup> <sub>vt</sub>                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
| Brinzolamid            | 0                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
| Brokkoli               | 4                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
| Indol-3-carbinol       | 1                         | Pgp <sup>1</sup> <sub>r</sub>                                       | Pgp <sup>1</sup> <sub>r</sub>                                               |                                                                 |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
| Isothiocyanat          | 70                        |                                                                     | MRP1,<br>MRP2 <sup>2</sup> <sub>vt</sub>                                    |                                                                 | X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub> | X <sup>5</sup> <sub>vt</sub> |                  |                  |                   | X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub>   | kein Substrat von Pgp <sup>5</sup> <sub>vt</sub><br>kein Inhibitor von Pgp <sup>6</sup> <sub>vt</sub> |                                    |
| Bromazepam             | 2                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   | X <sup>1</sup> <sub>vt</sub>                                   |                                                                                                       |                                    |
| Bromocriptin           | 7                         |                                                                     | Pgp, pgp2-/<br>mdr1b-<br>mRNA <sup>1</sup> <sub>vt</sub>                    | X <sup>2</sup> <sub>t, vt</sub><br>X <sup>3</sup> <sub>vt</sub> |                                                              |                              |                  |                  |                   | X <sup>4</sup> <sub>t</sub><br>X <sup>5</sup> <sub>vt</sub>    |                                                                                                       |                                    |
| Budesonid              | 10                        | Pgp <sup>1</sup> <sub>vt</sub><br>ATPase <sup>2</sup> <sub>vt</sub> |                                                                             |                                                                 |                                                              |                              |                  |                  |                   | X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>h</sub>    |                                                                                                       |                                    |
| Bufuralol              | 0                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
| Bupivacain             | 3                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   | X <sup>1</sup> <sub>t</sub><br>X <sup>2</sup> <sub>vt, t</sub> | Transport durch Pgp von<br>untergeordneter Bedeu-<br>tung <sup>2</sup> <sub>vt</sub>                  | Quinidin <sup>1</sup> <sub>t</sub> |
| Buprenorphin           | 2                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   | X <sup>1</sup> <sub>t</sub>                                    | kein Substrat <sup>2</sup> <sub>h</sub>                                                               |                                    |
| Bupropion              | 4                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   | X <sup>1</sup> <sub>vt</sub>                                   | sehr schwaches Substrat                                                                               |                                    |
| Buspiron               | 4                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
| Busulfan               | 6                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   | X <sup>1</sup> <sub>vt</sub>                                   | kein Substrat <sup>2</sup> <sub>vt</sub>                                                              |                                    |
| <b>Substanz</b>        | <b>Anzahl<br/>Artikel</b> | <b>Wirkung auf<br/>Funktion<br/>von</b>                             | <b>Wirkung auf<br/>Expression<br/>von</b>                                   | <b>MDR-<br/>Umkehr</b>                                          | <b>MRP<br/>1</b>                                             | <b>MRP<br/>2</b>             | <b>MRP<br/>3</b> | <b>MRP<br/>4</b> | <b>BCRP<br/>1</b> | <b>Pgp</b>                                                     | <b>Zusatz</b>                                                                                         | <b>Wechsel-<br/>wirkungen</b>      |
| Cafergot               | 0                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
| Calcitriol<br>(Vit. D) | 6                         | Pgp <sup>1</sup> <sub>vt</sub>                                      | MDR1-<br>mRNA <sup>2</sup> <sub>vt</sub><br>Mrp1 <sup>3</sup> <sub>vt</sub> |                                                                 |                                                              |                              |                  |                  |                   |                                                                | in LS180-Zellen <sup>2</sup> <sub>vt</sub>                                                            |                                    |
| Candesartan            | 0                         |                                                                     |                                                                             |                                                                 |                                                              |                              |                  |                  |                   |                                                                |                                                                                                       |                                    |
| Capsaicin              | 6                         | Pgp <sup>1</sup> <sub>vt</sub>                                      |                                                                             |                                                                 |                                                              |                              |                  |                  |                   | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub>   |                                                                                                       |                                    |

|                              |     |                                                                                                                    |                                                                                                                            |                                                              |                                    |                                                            |  |                              |                              |                                                                                                                                   |                                                                                                                                                                                                                                              |                                      |
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|                              |     |                                                                                                                    |                                                                                                                            |                                                              |                                    |                                                            |  |                              |                              | X <sup>4</sup> <sub>vt</sub>                                                                                                      |                                                                                                                                                                                                                                              |                                      |
| Captopril                    | 0   |                                                                                                                    |                                                                                                                            |                                                              |                                    |                                                            |  |                              |                              |                                                                                                                                   |                                                                                                                                                                                                                                              |                                      |
| Carbamazepin                 | 38  | Pgp <sup>1</sup> <sub>vt</sub>                                                                                     | Pgp <sup>2</sup> <sub>vt</sub><br>Pgp <sup>3</sup> <sub>vt</sub><br>MDR1-mRNA,<br>MRP2/MRP2-mRNA <sup>4</sup> <sub>h</sub> |                                                              | X <sup>5</sup> <sub>t</sub>        | X <sup>6</sup> <sub>t</sub><br>X <sup>7</sup> <sub>h</sub> |  |                              |                              | X <sup>8</sup> <sub>t</sub><br>X <sup>9</sup> <sub>vt</sub>                                                                       | kein Substrat <sup>10</sup> <sub>t, vt</sub><br><sup>11</sup> <sub>vt,t</sub> , <sup>12</sup> <sub>vt</sub> , <sup>13</sup> <sub>vt</sub><br>kein Inhibitor/Substrat <sup>14</sup> <sub>vt</sub><br>kein Induktor <sup>15</sup> <sub>h</sub> |                                      |
| Carisoprodol                 | 0   |                                                                                                                    |                                                                                                                            |                                                              |                                    |                                                            |  |                              |                              |                                                                                                                                   |                                                                                                                                                                                                                                              |                                      |
| Carmustin/<br>BCNU           | 27  |                                                                                                                    |                                                                                                                            |                                                              |                                    |                                                            |  |                              |                              | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub>                                      |                                                                                                                                                                                                                                              |                                      |
| Carteolol                    | 0   |                                                                                                                    |                                                                                                                            |                                                              |                                    |                                                            |  |                              |                              |                                                                                                                                   |                                                                                                                                                                                                                                              |                                      |
| Carvedilol                   | 17  |                                                                                                                    |                                                                                                                            | X <sup>1</sup> <sub>vt</sub>                                 |                                    |                                                            |  |                              |                              | X <sup>2</sup> <sub>vt, t</sub><br>X <sup>3</sup> <sub>vt, vt</sub><br>X <sup>4</sup> <sub>h</sub> , X <sup>5</sup> <sub>vt</sub> | Modulator <sup>6</sup> <sub>h</sub>                                                                                                                                                                                                          |                                      |
| Celecoxib                    | 12  | Pgp <sup>1</sup> <sub>vt</sub><br>Pgp <sup>2</sup> <sub>vt</sub><br>Pgp <sup>3</sup> <sub>vt, 4</sub> <sub>t</sub> | Pgp <sup>5</sup> <sub>vt, 6</sub> <sub>t</sub><br>MRP1 <sup>7</sup> <sub>vt</sub>                                          | X <sup>8</sup> <sub>vt</sub>                                 |                                    |                                                            |  | X <sup>9</sup> <sub>vt</sub> |                              |                                                                                                                                   |                                                                                                                                                                                                                                              |                                      |
| Cerivastatin                 | 6   | MDR1 <sup>1</sup> <sub>vt</sub>                                                                                    |                                                                                                                            |                                                              |                                    | X <sup>2</sup> <sub>vt</sub>                               |  |                              | X <sup>3</sup> <sub>vt</sub> | X <sup>4</sup> <sub>t, vt</sub><br>X <sup>5</sup> <sub>vt</sub>                                                                   |                                                                                                                                                                                                                                              |                                      |
| Cetirizin                    | 10  |                                                                                                                    |                                                                                                                            |                                                              |                                    |                                                            |  |                              |                              | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>t, vt</sub><br>X <sup>3</sup> <sub>t</sub>                                    |                                                                                                                                                                                                                                              | Ivermectin <sup>3</sup> <sub>t</sub> |
| Levocetirizin                |     |                                                                                                                    |                                                                                                                            |                                                              |                                    |                                                            |  |                              |                              | X <sup>1</sup> <sub>h</sub>                                                                                                       |                                                                                                                                                                                                                                              |                                      |
| R-Cetirizin                  |     |                                                                                                                    | MDR1 <sup>1</sup> <sub>vt</sub>                                                                                            |                                                              |                                    |                                                            |  |                              |                              |                                                                                                                                   |                                                                                                                                                                                                                                              |                                      |
| S-Cetirizin                  | 5   |                                                                                                                    | MDR1 <sup>1</sup> <sub>vt</sub>                                                                                            |                                                              |                                    |                                                            |  |                              |                              |                                                                                                                                   |                                                                                                                                                                                                                                              |                                      |
| Chinidin<br>(Quinidin)       | 270 |                                                                                                                    |                                                                                                                            | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> | X <sup>3</sup> <sub>t, h, vt</sub> |                                                            |  |                              |                              | X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>t, t</sub> , X <sup>7</sup> <sub>t</sub>      | kein Inhibitor in<br>Plazenta <sup>8</sup> <sub>vt, h</sub>                                                                                                                                                                                  |                                      |
| R-Diastereomer<br>Chinidin   |     |                                                                                                                    |                                                                                                                            |                                                              |                                    |                                                            |  |                              |                              | X <sup>1</sup> <sub>h</sub>                                                                                                       |                                                                                                                                                                                                                                              |                                      |
| S-Diastereomer<br>Chinidin   |     |                                                                                                                    |                                                                                                                            |                                                              |                                    |                                                            |  |                              |                              | X <sup>1</sup> <sub>vt</sub>                                                                                                      | schwacher Inhibitor                                                                                                                                                                                                                          |                                      |
| N-Alkylation<br>von Chinidin |     |                                                                                                                    |                                                                                                                            |                                                              |                                    |                                                            |  |                              |                              | X <sup>1</sup> <sub>t</sub>                                                                                                       |                                                                                                                                                                                                                                              |                                      |

|                            |    |                                                                       |                                                                   |                                                                                                                                                                                              |  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                            |                                                                                                                                         |
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| N-methyl-Chinidin          |    |                                                                       |                                                                   |                                                                                                                                                                                              |  |  |  |  |  | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                            |                                                                                                                                         |
| L-Valin Ester von Chinidin |    |                                                                       |                                                                   |                                                                                                                                                                                              |  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | kein Substrat <sup>1</sup> <sub>vt</sub> , <sup>2</sup> <sub>vt</sub>                                                                                      |                                                                                                                                         |
| Chinin (Quinin)            | 85 |                                                                       | mdr1 <sup>1</sup> <sub>vt</sub>                                   | X <sup>2</sup> <sub>h</sub><br>X <sup>3</sup> <sub>vt</sub>                                                                                                                                  |  |  |  |  |  | X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | „gering“ <sup>1</sup> <sub>vt</sub><br>„relativ schwach“ <sup>4</sup> <sub>vt</sub><br>Keine Interaktion mit Pgp <sup>6</sup> <sub>vt</sub>                |                                                                                                                                         |
| Chinin-10,11-Epoxid        |    |                                                                       |                                                                   |                                                                                                                                                                                              |  |  |  |  |  | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                            |                                                                                                                                         |
| Chlorambucil               | 31 |                                                                       | MRP1-mRNA <sup>1</sup> <sub>vt</sub> , <sup>2</sup> <sub>vt</sub> |                                                                                                                                                                                              |  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                            |                                                                                                                                         |
| Chloramphenicol            | 51 |                                                                       |                                                                   |                                                                                                                                                                                              |  |  |  |  |  | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                            |                                                                                                                                         |
| Chlordiazepoxid            | 2  | ATPase <sup>1</sup> <sub>vt</sub>                                     |                                                                   |                                                                                                                                                                                              |  |  |  |  |  | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                            |                                                                                                                                         |
| Chloroquin                 | 88 | Pgp <sup>1</sup> <sub>vt</sub><br>Pgp.Mrp1 <sup>2</sup> <sub>vt</sub> |                                                                   | X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub>                                                                                                                                 |  |  |  |  |  | X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Modulator <sup>5</sup> <sub>vt</sub><br>Modulator <sup>6</sup> <sub>vt</sub>                                                                               | HIV-Protease-Inhibitoren <sup>7</sup> <sub>vt</sub><br>Fluoxetin <sup>8</sup> <sub>vt</sub><br>Roxythromycin <sup>9</sup> <sub>vt</sub> |
| Chlorpheniramin            | 4  |                                                                       |                                                                   |                                                                                                                                                                                              |  |  |  |  |  | X <sup>1</sup> <sub>t</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                            |                                                                                                                                         |
| Chlorpromazin              | 31 | Pgp <sup>1</sup> <sub>vt</sub>                                        |                                                                   | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub> |  |  |  |  |  | X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>vt</sub><br>X <sup>13</sup> <sub>vt</sub><br>X <sup>14</sup> <sub>vt</sub><br>X <sup>15</sup> <sub>vt</sub><br>X <sup>16</sup> <sub>vt</sub><br>X <sup>17</sup> <sub>t</sub><br>X <sup>18</sup> <sub>t</sub><br>X <sup>19</sup> <sub>t</sub><br>X <sup>20</sup> <sub>t</sub><br>X <sup>21</sup> <sub>vt</sub><br>X <sup>22</sup> <sub>t</sub><br>X <sup>23</sup> <sub>r</sub> | Phosphatidylcholin/-serin <sup>26</sup> <sub>vt</sub><br>Quinidin <sup>27</sup> <sub>t</sub><br>Äthinyl-östradiol, Progesteron <sup>28</sup> <sub>vt</sub> |                                                                                                                                         |

|                                             |     |  |                                                                                                     |                              |  |  |  |  |                                                              |                                                                                                                                                                                                                                |                                                                                                         |                                                                                                                                                                |
|---------------------------------------------|-----|--|-----------------------------------------------------------------------------------------------------|------------------------------|--|--|--|--|--------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                             |     |  |                                                                                                     |                              |  |  |  |  |                                                              | X <sup>24</sup> <sub>vt</sub><br>X <sup>25</sup> <sub>vt</sub>                                                                                                                                                                 |                                                                                                         |                                                                                                                                                                |
| Chlorpropamid                               | 0   |  |                                                                                                     |                              |  |  |  |  |                                                              |                                                                                                                                                                                                                                |                                                                                                         |                                                                                                                                                                |
| Chlorzoxazon                                | 0   |  |                                                                                                     |                              |  |  |  |  |                                                              |                                                                                                                                                                                                                                |                                                                                                         |                                                                                                                                                                |
| Cholecalciferol                             | 10  |  | Pgp <sup>1</sup> <sub>vt</sub><br>MDR1 <sup>2</sup> <sub>vt</sub><br>MRP <sup>3</sup> <sub>vt</sub> |                              |  |  |  |  |                                                              | X <sup>4</sup> <sub>h</sub><br>X <sup>5</sup> <sub>vt</sub>                                                                                                                                                                    |                                                                                                         |                                                                                                                                                                |
| CPGS                                        |     |  |                                                                                                     |                              |  |  |  |  |                                                              | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                   | “Cholecalciferol- poly-<br>ethylen-glycolsuccinat”                                                      |                                                                                                                                                                |
| Ciclosporin A<br>-siehe Cyclospo-<br>rin A- | 734 |  |                                                                                                     |                              |  |  |  |  |                                                              |                                                                                                                                                                                                                                |                                                                                                         |                                                                                                                                                                |
| Cimetidin                                   | 49  |  |                                                                                                     |                              |  |  |  |  | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> | X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt, t</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>h</sub> | kein Substrat <sup>10</sup> <sub>vt</sub><br>kein Substrat von<br>MRP2, Pgp <sup>11</sup> <sub>vt</sub> | Zolmitriptan <sup>12</sup> <sub>vt</sub><br>Itraconazol <sup>13</sup> <sub>h</sub>                                                                             |
| Cinnarizin                                  | 0   |  |                                                                                                     |                              |  |  |  |  |                                                              |                                                                                                                                                                                                                                |                                                                                                         |                                                                                                                                                                |
| Ciprofloxacin                               | 26  |  |                                                                                                     | X <sup>1</sup> <sub>vt</sub> |  |  |  |  | X <sup>2</sup> <sub>h, vt</sub>                              |                                                                                                                                                                                                                                | kein Substrat <sup>3</sup> <sub>vt</sub><br>kein Substrat von MDR1,<br>MRP2 <sup>4</sup> <sub>vt</sub>  | Grepa-<br>floxacin <sup>4</sup> <sub>vt</sub><br>Orangensaft mit<br>Kalzium<br>angereichert <sup>5</sup> <sub>r</sub>                                          |
| CNV97100                                    |     |  |                                                                                                     |                              |  |  |  |  |                                                              | X <sup>6</sup> <sub>vt</sub>                                                                                                                                                                                                   |                                                                                                         |                                                                                                                                                                |
| Cisaprid                                    | 5   |  |                                                                                                     |                              |  |  |  |  |                                                              |                                                                                                                                                                                                                                |                                                                                                         |                                                                                                                                                                |
| Citalopram                                  | 8   |  |                                                                                                     |                              |  |  |  |  |                                                              | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>t</sub>                                                                                                                                                                    | “schwach” <sup>1</sup>                                                                                  |                                                                                                                                                                |
| Clarithromycin                              | 34  |  |                                                                                                     |                              |  |  |  |  |                                                              | X <sup>1</sup> <sub>r</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>h</sub><br>X <sup>4</sup> <sub>h</sub><br>X <sup>5</sup> <sub>h</sub><br>X <sup>6</sup> <sub>h</sub>                                        |                                                                                                         | Digoxin <sup>11</sup> <sub>r</sub><br>Simvastatin <sup>12</sup> <sub>h</sub><br>Sirolimus <sup>13</sup> <sub>h</sub><br>Rifampin <sup>14</sup> <sub>reop</sub> |

|                             |     |  |                                |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
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|                             |     |  |                                |  |  |  |  |  |  | X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>h</sub><br>X <sup>9</sup> <sub>h</sub><br>X <sup>10</sup> <sub>vt</sub>                                                                                                 |  |                                                                                                                                                                                                                                                                                                       |
| Clemastin                   | 0   |  |                                |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Clobazam                    | 0   |  |                                |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Clofibrat                   | 2   |  | mdr2 <sup>1</sup> <sub>t</sub> |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Clomipramin                 | 3   |  |                                |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Clonazepam                  | 0   |  |                                |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Clonidin                    | 2   |  |                                |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Clopidogrel                 | 137 |  |                                |  |  |  |  |  |  | X <sup>1</sup> <sub>h, vt</sub>                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Clorazepat                  | 0   |  |                                |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Clotrimazol                 | 6   |  |                                |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Clozapin                    | 10  |  | Pgp <sup>1</sup> <sub>vt</sub> |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Cocain                      | 3   |  |                                |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Codein                      | 7   |  |                                |  |  |  |  |  |  | X <sup>1</sup> <sub>r</sub>                                                                                                                                                                                                 |  |                                                                                                                                                                                                                                                                                                       |
| Coffein                     | 15  |  |                                |  |  |  |  |  |  |                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                                                                                       |
| Colchicin                   | 467 |  |                                |  |  |  |  |  |  | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>r</sub><br>X <sup>5</sup> <sub>t</sub><br>X <sup>6</sup> <sub>h</sub>                                    |  | Atorvastatin <sup>6</sup> <sub>h</sub><br>Verapamil <sup>7</sup> <sub>h</sub><br>Chlorpro-<br>mazin <sup>8</sup> <sub>vt</sub><br>Erythromycin,<br>Josamycin,<br>Clarithro-<br>mycin <sup>9</sup> <sub>h, 10</sub> <sub>r</sub><br>Glukokortikoid,<br>Tricho-<br>statin A <sup>11</sup> <sub>vt</sub> |
| Cortisol<br>(Hydrocortison) | 113 |  | Pgp <sup>1</sup> <sub>vt</sub> |  |  |  |  |  |  | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>t</sub> |  | Anti-<br>depressiva <sup>11</sup> <sub>r, vt</sub>                                                                                                                                                                                                                                                    |

|                  |                |                                |                               |                                                                                              |                              |                              |                              |       |                              | X <sup>9</sup> <sub>h</sub><br>X <sup>10</sup> <sub>vt</sub>                                                                                                                                                                                         |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
|------------------|----------------|--------------------------------|-------------------------------|----------------------------------------------------------------------------------------------|------------------------------|------------------------------|------------------------------|-------|------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cortison         | 3              |                                |                               |                                                                                              |                              |                              |                              |       |                              |                                                                                                                                                                                                                                                      |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
| Cumarin          | 20             |                                |                               | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub> |                              |                              |                              |       |                              | X <sup>1</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub>                                                                                                                         |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
| Cyclobenzaprin   | 0              |                                |                               |                                                                                              |                              |                              |                              |       |                              |                                                                                                                                                                                                                                                      |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
| Cyclo-phosphamid | 137            |                                |                               |                                                                                              |                              |                              |                              |       |                              | X <sup>1</sup> <sub>h</sub>                                                                                                                                                                                                                          | kein Substrat <sup>2</sup> <sub>t</sub> |                                                                                                                                                                                                                                                                                                                                                                                    |
| Cyclosporin A    | 1300           |                                | Pgp <sup>1</sup> <sub>h</sub> | X <sup>2</sup> <sub>h</sub>                                                                  |                              |                              |                              |       |                              | X <sup>1</sup> <sub>h</sub><br>X <sup>3</sup> <sub>h</sub><br>X <sup>4</sup> <sub>h</sub><br>X <sup>5</sup> <sub>h</sub><br>X <sup>6</sup> <sub>h</sub><br>X <sup>7</sup> <sub>h</sub><br>X <sup>8</sup> <sub>h</sub><br>X <sup>9</sup> <sub>r</sub> |                                         | Sirolimus <sup>9</sup> <sub>r</sub><br>Amlodipin <sup>10</sup> <sub>h</sub><br>Grapefruit-Saft <sup>11</sup> <sub>h</sub><br>Carvedilol <sup>12</sup> <sub>h</sub><br>St John's wort <sup>13</sup> <sub>h</sub> , <sup>14</sup> <sub>r</sub> , <sup>15</sup> <sub>r</sub><br>Clarithromycin <sup>16</sup> <sub>vt</sub><br>Fluorchinolone,<br>Makrolide <sup>17</sup> <sub>r</sub> |
| Substanz         | Anzahl Artikel | Wirkung auf Funktion von       | Wirkung auf Expression von    | MDR-Umkehr                                                                                   | MRP 1                        | MRP 2                        | MRP 3                        | MRP 4 | BCRP 1                       | Pgp                                                                                                                                                                                                                                                  | Zusatz                                  | Wechselwirkungen                                                                                                                                                                                                                                                                                                                                                                   |
| Dacarbazin       | 9              |                                |                               |                                                                                              |                              |                              |                              |       |                              |                                                                                                                                                                                                                                                      |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
| Danazol          | 3              |                                |                               |                                                                                              |                              |                              |                              |       |                              |                                                                                                                                                                                                                                                      |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
| Dantrolen        | 2              |                                |                               |                                                                                              |                              |                              |                              |       | X <sup>1</sup> <sub>vt</sub> |                                                                                                                                                                                                                                                      |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
| Dapson           | 0              |                                |                               |                                                                                              |                              |                              |                              |       |                              |                                                                                                                                                                                                                                                      |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
| Debrisoquin      | 0              |                                |                               |                                                                                              |                              |                              |                              |       |                              |                                                                                                                                                                                                                                                      |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
| Delaviridin      | 10             | Pgp <sup>1</sup> <sub>vt</sub> |                               |                                                                                              | X <sup>2</sup> <sub>vt</sub> | X <sup>2</sup> <sub>vt</sub> | X <sup>2</sup> <sub>vt</sub> |       | X <sup>3</sup> <sub>vt</sub> | X <sup>4</sup> <sub>vt</sub>                                                                                                                                                                                                                         |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
| Desipramin       | 9              |                                |                               |                                                                                              |                              |                              |                              |       |                              | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>t</sub>                                                                                                                                                                                          |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
| Desogestrel      | 2              |                                |                               |                                                                                              |                              |                              |                              |       |                              | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                         |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |
| Dexamethason     | 152            |                                |                               |                                                                                              |                              |                              |                              |       |                              | X <sup>1</sup> <sub>r</sub><br>X <sup>2</sup> <sub>r</sub>                                                                                                                                                                                           |                                         |                                                                                                                                                                                                                                                                                                                                                                                    |

|                       |     |                                   |  |  |  |  |  |                                                              |  |                                                                                                                                                                                         |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
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|                       |     |                                   |  |  |  |  |  |                                                              |  | X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub>                                                                                                                            |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Dexfenfluramin        | 0   |                                   |  |  |  |  |  |                                                              |  |                                                                                                                                                                                         |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Dextromethorphan      | 10  |                                   |  |  |  |  |  |                                                              |  | X <sup>1</sup> <sub>t</sub>                                                                                                                                                             | kein Substrat <sup>2</sup> <sub>t</sub><br>kein Substrat <sup>3</sup> <sub>vt</sub> | Grapefruit-/Orangensaft <sup>4</sup> <sub>h</sub><br>Verapamil <sup>5</sup> <sub>t</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Diazepam              | 14  | ATPase <sup>1</sup> <sub>vt</sub> |  |  |  |  |  |                                                              |  | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>t</sub><br>X <sup>3</sup> <sub>t</sub>                                                                                              |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Diclofenac            | 6   |                                   |  |  |  |  |  | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> |  | X <sup>3</sup> <sub>vt</sub>                                                                                                                                                            |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Dicloxacillin         | 2   |                                   |  |  |  |  |  |                                                              |  | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>h</sub>                                                                                                                             |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Dicumarol             | 2   |                                   |  |  |  |  |  |                                                              |  |                                                                                                                                                                                         |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Didanosin             | 8   |                                   |  |  |  |  |  |                                                              |  |                                                                                                                                                                                         |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Diethyldithiocarbamat | 8   |                                   |  |  |  |  |  |                                                              |  | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                            |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Digitoxin             | 11  |                                   |  |  |  |  |  |                                                              |  | X <sup>1</sup> <sub>t</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>h</sub>                                                              | Modulator <sup>5</sup> <sub>vt</sub>                                                | Verapamil <sup>6</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Digoxin               | 335 |                                   |  |  |  |  |  |                                                              |  | X <sup>1</sup> <sub>r</sub><br>X <sup>2</sup> <sub>r</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>r</sub><br>X <sup>5</sup> <sub>r</sub><br>X <sup>6</sup> <sub>vt</sub> |                                                                                     | Carvedilol <sup>6</sup> <sub>vt</sub><br>St John`s wort <sup>7</sup> <sub>cop</sub> , <sup>8</sup> <sub>r</sub> ,<br><sup>9</sup> <sub>r</sub> , <sup>10</sup> <sub>r</sub> , <sup>11</sup> <sub>r</sub><br>Ranolazin <sup>12</sup> <sub>r</sub><br>Rifampin <sup>13</sup> <sub>r</sub> ,<br><sub>cop</sub><br>Doxazosin,<br>Ketoconazol,<br>Itraconazol,<br>Miconazol <sup>14</sup> <sub>vt</sub><br>Mifepriston <sup>15</sup> <sub>vt</sub><br>Rifampin <sup>16</sup> <sub>vt</sub><br>Rifampicin,<br>Penytoin,<br>Telmisartan <sup>17</sup> <sub>vt</sub> |

|                  |    |  |                                                                                                    |                                                                                             |  |  |  |  |  |                                                                                                                                                                                                                             |                                                                                                                                |                                                                                                                                                                                                        |
|------------------|----|--|----------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                  |    |  |                                                                                                    |                                                                                             |  |  |  |  |  |                                                                                                                                                                                                                             |                                                                                                                                | Clarithromycin <sup>18h, 19h, 20h, 21h, 22h</sup><br>Rifampin,<br>Clarithromycin <sup>23h, 24h</sup><br>St John's wort,<br>Rifampin,<br>Clarithromycin <sup>25h</sup><br>Amiodaron <sup>26r, 27t</sup> |
| Dihydrocodein    | 0  |  |                                                                                                    |                                                                                             |  |  |  |  |  |                                                                                                                                                                                                                             |                                                                                                                                |                                                                                                                                                                                                        |
| Dihydroergotamin | 0  |  |                                                                                                    |                                                                                             |  |  |  |  |  |                                                                                                                                                                                                                             |                                                                                                                                |                                                                                                                                                                                                        |
| Diltiazem        | 48 |  |                                                                                                    | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>r</sub> |  |  |  |  |  | X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>r</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>r</sub> | Desacetyl-Diltiazem ist Substrat von Pgp <sup>10</sup> <sub>vt</sub><br>Kein Einfluss auf Pgp-Aktivität in vivo <sup>11h</sup> | Verapamil <sup>12</sup> <sub>vt</sub><br>Tacrolimus <sup>13</sup> <sub>h</sub><br>Grapefruit-saft <sup>14</sup> <sub>hcop</sub><br>Quercetin <sup>15</sup> <sub>t</sub>                                |
| Dimethylsulfoxid | 14 |  | Pgp <sup>1</sup> <sub>vt</sub><br>Pgp <sup>2</sup> <sub>vt</sub><br>Pgp <sup>3</sup> <sub>vt</sub> |                                                                                             |  |  |  |  |  | X <sup>4</sup> <sub>vt</sub>                                                                                                                                                                                                |                                                                                                                                |                                                                                                                                                                                                        |
| Diphenhydramin   | 6  |  |                                                                                                    |                                                                                             |  |  |  |  |  |                                                                                                                                                                                                                             |                                                                                                                                |                                                                                                                                                                                                        |
| Disopyramid      | 2  |  |                                                                                                    |                                                                                             |  |  |  |  |  |                                                                                                                                                                                                                             |                                                                                                                                | Grapefruit-saft <sup>1</sup> <sub>rcop</sub>                                                                                                                                                           |
| Disulfiram       | 7  |  |                                                                                                    |                                                                                             |  |  |  |  |  | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                | Modulator von MDR1, MRP1 <sup>2</sup> <sub>vt</sub>                                                                            |                                                                                                                                                                                                        |
| Dithiocarbamat   | 3  |  |                                                                                                    |                                                                                             |  |  |  |  |  |                                                                                                                                                                                                                             |                                                                                                                                |                                                                                                                                                                                                        |
| Dolasetron       | 1  |  |                                                                                                    |                                                                                             |  |  |  |  |  |                                                                                                                                                                                                                             |                                                                                                                                |                                                                                                                                                                                                        |
| Domperidon       | 6  |  |                                                                                                    |                                                                                             |  |  |  |  |  | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>t</sub><br>X <sup>3</sup> <sub>t,vt</sub>                                                                                                                               |                                                                                                                                | Cyclosporin A <sup>3</sup> <sub>t, vt</sub><br>Quinidin, Grapefruit-saft <sup>4</sup> <sub>vt</sub>                                                                                                    |



|                  |                |                                |                                                                   |            |                              |                              |                              |       |                              | X <sup>4</sup> <sub>vt</sub>                                                                 |                                                                                                                                            |                                                                                                                                                                                                     |
|------------------|----------------|--------------------------------|-------------------------------------------------------------------|------------|------------------------------|------------------------------|------------------------------|-------|------------------------------|----------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Donepezil        | 1              |                                |                                                                   |            |                              |                              |                              |       |                              | X <sup>1</sup> <sub>t</sub>                                                                  |                                                                                                                                            |                                                                                                                                                                                                     |
| Dorzolamid       | 0              |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            |                                                                                                                                                                                                     |
| Doxepin          | 2              |                                |                                                                   |            |                              |                              |                              |       |                              | X <sup>1</sup> <sub>t</sub>                                                                  |                                                                                                                                            |                                                                                                                                                                                                     |
| Doxorubicin      | 2186           |                                | Pgp <sup>1</sup> <sub>vt</sub>                                    |            |                              |                              |                              |       |                              | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub> | MDR-Umkehr durch<br>„liposomal encapsulated<br>doxorubicin“ <sup>5</sup> <sub>r</sub>                                                      | Cyclosporin<br>A <sup>6</sup> <sub>t</sub> , <sup>7</sup> <sub>t</sub><br>Flezelastin,<br>Azela <sup>8</sup> <sub>vt</sub><br>Bexaroten <sup>9</sup> <sub>vt</sub> ,<br><sup>10</sup> <sub>vt</sub> |
| Doxycyclin       | 7              |                                | MDR3 <sup>1</sup> <sub>vt</sub><br>Pgp <sup>2</sup> <sub>vt</sub> |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            |                                                                                                                                                                                                     |
| Drospirenon      | 0              |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            |                                                                                                                                                                                                     |
| Duloxetin        | 0              |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            |                                                                                                                                                                                                     |
|                  |                |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            |                                                                                                                                                                                                     |
| Substanz         | Anzahl Artikel | Wirkung auf Funktion von       | Wirkung auf Expression von                                        | MDR-Umkehr | MRP 1                        | MRP 2                        | MRP 3                        | MRP 4 | BCRP 1                       | Pgp                                                                                          | Zusatz                                                                                                                                     | Wechselwirkungen                                                                                                                                                                                    |
| Econazol         | 0              |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            |                                                                                                                                                                                                     |
| “Ecstasy” (MDMA) | 6              |                                |                                                                   |            |                              |                              |                              |       |                              | X <sup>1</sup> <sub>vt</sub>                                                                 | durch Pgp ermöglichte Aufnahme in Gehirn <sup>2</sup> <sub>t</sub><br>kein Substrat <sup>3</sup> <sub>vt</sub> , <sup>4</sup> <sub>t</sub> |                                                                                                                                                                                                     |
| Efavirenz        | 18             | Pgp <sup>1</sup> <sub>vt</sub> | Pgp <sup>1</sup> <sub>vt</sub>                                    |            | X <sup>2</sup> <sub>vt</sub> | X <sup>2</sup> <sub>vt</sub> | X <sup>2</sup> <sub>vt</sub> |       | X <sup>3</sup> <sub>vt</sub> | X <sup>4</sup> <sub>h</sub><br>X <sup>5</sup> <sub>vt</sub>                                  | kein Substrat/<br>Induktor/Inhibitor <sup>6</sup> <sub>vt</sub>                                                                            |                                                                                                                                                                                                     |
| Eletriptan       | 3              |                                |                                                                   |            |                              |                              |                              |       |                              | X <sup>1</sup> <sub>h</sub><br>X <sup>2</sup> <sub>vt</sub>                                  |                                                                                                                                            |                                                                                                                                                                                                     |
| Enalapril        | 3              |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              | Enalapril ist Substrat von Pgp <sup>1</sup> <sub>vt</sub>                                                                                  |                                                                                                                                                                                                     |
| Encainid         | 1              |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            |                                                                                                                                                                                                     |
| Enfluran         | 0              |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            |                                                                                                                                                                                                     |
| Enoxacin         | 5              |                                |                                                                   |            |                              |                              |                              |       |                              | X <sup>1</sup> <sub>vt</sub>                                                                 |                                                                                                                                            |                                                                                                                                                                                                     |
| Entacapon        | 0              |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            |                                                                                                                                                                                                     |
| Eplerenon        | 0              |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            |                                                                                                                                                                                                     |
| Eprosartan       | 0              |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            |                                                                                                                                                                                                     |
| Ergotamin        | 2              |                                |                                                                   |            |                              |                              |                              |       |                              |                                                                                              |                                                                                                                                            | Grapefruitsaft <sup>1</sup> <sub>reop</sub>                                                                                                                                                         |

|                                                        |                           |                                         |                                           |                        |                  |                  |                  |                  |                   |                                                                   |                                                                                                |                                                                                                                                                                                                                                      |
|--------------------------------------------------------|---------------------------|-----------------------------------------|-------------------------------------------|------------------------|------------------|------------------|------------------|------------------|-------------------|-------------------------------------------------------------------|------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Erythromycin                                           | 121                       |                                         |                                           |                        |                  |                  |                  |                  |                   | $X_r^1$<br>$X_r^2$<br>$X_h^3$<br>$X_h^4$<br>$X_{vt}^5$<br>$X_t^6$ |                                                                                                | Atorvastatin <sup>7</sup> <sub>r</sub><br>cop<br>St John`s wort <sup>8</sup> <sub>r</sub><br>Sirolimus <sup>9</sup> <sub>r</sub><br>Simvastatin <sup>10</sup> <sub>h</sub><br>Fluorchinolon,<br>Makrolide <sup>11</sup> <sub>r</sub> |
| Escitalopram                                           | 2                         |                                         |                                           |                        |                  |                  |                  |                  |                   | $X_{vt}^1$                                                        | “vernachlässigbar”                                                                             |                                                                                                                                                                                                                                      |
| Esomoeprazol                                           | 17                        |                                         |                                           |                        |                  |                  |                  |                  |                   | $X_h^1$                                                           |                                                                                                |                                                                                                                                                                                                                                      |
| Estradiol                                              | 34                        | Pgp <sup>1</sup> <sub>vt</sub>          |                                           |                        | $X_t^2$          | $X_{vt}^3$       | $X_{vt}^4$       | $X_t^5$          | $X_r^6$           |                                                                   | kein Substrat von Pgp <sup>7</sup> <sub>t</sub><br>Substrat von MRP5 <sup>8</sup> <sub>t</sub> |                                                                                                                                                                                                                                      |
| Ethanol<br>-siehe Äthanol-                             |                           |                                         |                                           |                        |                  |                  |                  |                  |                   |                                                                   |                                                                                                |                                                                                                                                                                                                                                      |
| Ethinyl-<br>estradiol<br>-siehe Äthinyl-<br>östradiol- |                           |                                         |                                           |                        |                  |                  |                  |                  |                   |                                                                   |                                                                                                |                                                                                                                                                                                                                                      |
| Ethosuximid                                            | 1                         |                                         |                                           |                        |                  |                  |                  |                  |                   |                                                                   |                                                                                                |                                                                                                                                                                                                                                      |
| Ethylestradiol                                         | 0                         |                                         |                                           |                        |                  |                  |                  |                  |                   |                                                                   |                                                                                                |                                                                                                                                                                                                                                      |
| Ethylmorphin                                           | 0                         |                                         |                                           |                        |                  |                  |                  |                  |                   |                                                                   |                                                                                                |                                                                                                                                                                                                                                      |
| Etonorgestrel                                          | 0                         |                                         |                                           |                        |                  |                  |                  |                  |                   |                                                                   |                                                                                                |                                                                                                                                                                                                                                      |
| Etoposid                                               | 573                       |                                         |                                           |                        | $X_{vt}^1$       |                  |                  |                  |                   | $X_{vt}^2$<br>$X_h^3$<br>$X_h^4$<br>$X_{vt}^5$<br>$X_t^6$         |                                                                                                | Prednison <sup>3</sup> <sub>h</sub><br>cop                                                                                                                                                                                           |
| Etoricoxib                                             | 0                         |                                         |                                           |                        |                  |                  |                  |                  |                   |                                                                   |                                                                                                |                                                                                                                                                                                                                                      |
| Exemestan                                              | 0                         |                                         |                                           |                        |                  |                  |                  |                  |                   |                                                                   |                                                                                                |                                                                                                                                                                                                                                      |
|                                                        |                           |                                         |                                           |                        |                  |                  |                  |                  |                   |                                                                   |                                                                                                |                                                                                                                                                                                                                                      |
| <b>Substanz</b>                                        | <b>Anzahl<br/>Artikel</b> | <b>Wirkung auf<br/>Funktion<br/>von</b> | <b>Wirkung auf<br/>Expression<br/>von</b> | <b>MDR-<br/>Umkehr</b> | <b>MRP<br/>1</b> | <b>MRP<br/>2</b> | <b>MRP<br/>3</b> | <b>MRP<br/>4</b> | <b>BCRP<br/>1</b> | <b>Pgp</b>                                                        | <b>Zusatz</b>                                                                                  | <b>Wechsel-<br/>wirkungen</b>                                                                                                                                                                                                        |
| Fasten                                                 | 0                         |                                         |                                           |                        |                  |                  |                  |                  |                   |                                                                   |                                                                                                |                                                                                                                                                                                                                                      |
| Felbamat                                               | 5                         |                                         |                                           |                        |                  |                  |                  |                  |                   | $X_t^1$<br>$X_r^2$<br>$X_r^3$                                     | kein Substrat <sup>4</sup> <sub>t</sub>                                                        |                                                                                                                                                                                                                                      |

|                                |     |                                                                                                     |                                |                                                              |                             |                             |  |  |  |                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                  |                                                                              |
|--------------------------------|-----|-----------------------------------------------------------------------------------------------------|--------------------------------|--------------------------------------------------------------|-----------------------------|-----------------------------|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| Felodipin                      | 18  |                                                                                                     |                                |                                                              |                             |                             |  |  |  | X <sup>1</sup> <sub>r</sub>                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                  |                                                                              |
| Fenofibrat                     | 4   |                                                                                                     | mdr2 <sup>1</sup> <sub>t</sub> |                                                              |                             |                             |  |  |  | X <sup>2</sup> <sub>t</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub>                                                                                                                                |                                                                                                                                                                                                                                                                                  |                                                                              |
| Fentanyl                       | 16  | Pgp ATPase <sup>1</sup> <sub>t</sub>                                                                |                                |                                                              |                             |                             |  |  |  | X <sup>2</sup> <sub>t</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>t</sub><br>X <sup>5</sup> <sub>h</sub>                                                                                                  |                                                                                                                                                                                                                                                                                  |                                                                              |
| Fexofenadin                    | 30  |                                                                                                     |                                |                                                              |                             |                             |  |  |  | X <sup>1</sup> <sub>h</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>h</sub><br>X <sup>4</sup> <sub>h</sub><br>X <sup>5</sup> <sub>h</sub><br>X <sup>6</sup> <sub>h</sub><br>X <sup>7</sup> <sub>h</sub>     | Verapamil <sup>4</sup> <sub>h</sub><br>Itraconazol <sup>5</sup> <sub>h</sub> , <sup>7</sup> <sub>h</sub><br>St John`s<br>wort <sup>8</sup> <sub>r</sub> , <sup>9</sup> <sub>r</sub><br>Lopinavir/<br>Ritonavir <sup>10</sup> <sub>h</sub><br>Rifampin <sup>11</sup> <sub>r</sub> |                                                                              |
| Finasterid                     | 1   |                                                                                                     |                                |                                                              |                             |                             |  |  |  |                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                  |                                                                              |
| Flavonoide<br>(Grapefruitsaft) | 227 | ATPase <sup>1</sup> <sub>vt</sub>                                                                   |                                | X <sup>2</sup> <sub>vt</sub>                                 |                             |                             |  |  |  | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>r</sub> |                                                                                                                                                                                                                                                                                  |                                                                              |
| Flecainid                      | 1   |                                                                                                     |                                |                                                              |                             |                             |  |  |  |                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                  |                                                                              |
| Fluconazol                     | 47  |                                                                                                     |                                |                                                              |                             |                             |  |  |  | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                  |                                                                              |
| Flunarizin                     | 3   |                                                                                                     |                                |                                                              |                             |                             |  |  |  |                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                  |                                                                              |
| Flunitrazepam                  | 1   |                                                                                                     |                                |                                                              |                             |                             |  |  |  |                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                  |                                                                              |
| Fluoruracil                    | 88  |                                                                                                     | MDR <sup>1</sup> <sub>vt</sub> |                                                              | X <sup>2</sup> <sub>r</sub> | X <sup>2</sup> <sub>r</sub> |  |  |  |                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                  | Gerbsäure <sup>3</sup> <sub>vt</sub><br>Lonafarnib <sup>2</sup> <sub>r</sub> |
| Fluoxetin                      | 11  |                                                                                                     |                                | X <sup>2</sup> <sub>vt</sub>                                 |                             |                             |  |  |  | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub>                                                                                                                               |                                                                                                                                                                                                                                                                                  |                                                                              |
| Flupentixol                    | 28  | PGP-ATPase <sup>1</sup> <sub>vt</sub><br>(cis-Flupentixol)<br>PGP-ATPase <sup>2</sup> <sub>vt</sub> |                                | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub> |                             |                             |  |  |  | X <sup>11</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>vt</sub>                                                                                                                                                             |                                                                                                                                                                                                                                                                                  |                                                                              |

|              |                |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
|--------------|----------------|--------------------------|--------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|--------------------------------------------------------------|--------------------------------------------------------------|--------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|-----------------------------------------------|
|              |                | (trans-Flupentixol)      |                                | X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>vt</sub> |                                                              |                                                              |                                                              |                                                              |                                                                                                                             | X <sup>13</sup> <sub>vt</sub><br>X <sup>14</sup> <sub>vt</sub><br>X <sup>15</sup> <sub>vt</sub><br>X <sup>16</sup> <sub>vt</sub><br>X <sup>17</sup> <sub>vt</sub>                            |           |                                               |
| Fluphenazin  | 9              |                          |                                | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                  |                                                              |                                                              |                                                              |                                                              |                                                                                                                             | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>r</sub>                                                                                                  |           |                                               |
| Flurazepam   | 2              |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                 |           |                                               |
| Flurbiprofen | 0              |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
| Flutamid     | 0              |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
| Fluticason   | 2              |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
| Fluvastatin  | 10             |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
| Fulvestrant  | 3              |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
| Fluvoxamin   | 10             |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                 |           |                                               |
| Formoterol   | 0              |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
| Fosphenytoin | 0              |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
| Furafylline  | 1              |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
|              |                |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
| Substanz     | Anzahl Artikel | Wirkung auf Funktion von | Wirkung auf Expression von     | MDR-Umkehr                                                                                                                                                                                                                    | MRP 1                                                        | MRP 2                                                        | MRP 3                                                        | MRP 4                                                        | BCRP 1                                                                                                                      | Pgp                                                                                                                                                                                          | Zusatz    | Wechselwirkungen                              |
| Galantamin   | 0              |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
| Gemfibrozil  | 11             |                          |                                |                                                                                                                                                                                                                               | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> |                                                                                                                             |                                                                                                                                                                                              |           | Cerivastatin <sup>3</sup> <sub>r</sub><br>cop |
| Gestoden     | 3              |                          |                                |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              |                                                                                                                             |                                                                                                                                                                                              |           |                                               |
| Gleevec      | 75             |                          | Pgp <sup>1</sup> <sub>vt</sub> |                                                                                                                                                                                                                               |                                                              |                                                              |                                                              |                                                              | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>t</sub> | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub> |           |                                               |
| Glibenclamid | 28             |                          |                                |                                                                                                                                                                                                                               | X <sup>1</sup> <sub>vt</sub>                                 |                                                              | X <sup>2</sup> <sub>vt</sub>                                 |                                                              | X <sup>2</sup> <sub>vt</sub>                                                                                                | X <sup>4</sup> <sub>vt</sub>                                                                                                                                                                 | Schwaches | Clarithro-                                    |

|                                           |                           |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
|-------------------------------------------|---------------------------|-----------------------------------------|----------------------------------------------------------------|------------------------------|------------------|------------------|------------------|------------------|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| (Glyburid)                                |                           |                                         |                                                                |                              |                  |                  |                  |                  | X <sup>3</sup> <sub>vt</sub> | X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>h</sub>                                                                 | Substrat von Pgp <sup>6</sup> <sub>vt</sub><br>Mögliches Substrat von<br>Pgp, Bcrp, Mrp <sup>8</sup> <sub>r</sub> | mycin <sup>7</sup> <sub>h</sub> Ri-<br>fampin <sup>9</sup> <sub>h</sub> <b>cop</b>              |
| Glimepirid                                | 0                         |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
| Glipizid                                  | 3                         |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   | Rifampin <sup>1</sup> <sub>h</sub> <b>cop</b>                                                   |
| Granisetron                               | 2                         |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
| Grapefruitsaft<br>-siehe Flavo-<br>noide- |                           |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
| Grisoefulvin                              | 2                         |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
| <b>Substanz</b>                           | <b>Anzahl<br/>Artikel</b> | <b>Wirkung auf<br/>Funktion<br/>von</b> | <b>Wirkung auf<br/>Expression<br/>von</b>                      | <b>MDR-<br/>Umkehr</b>       | <b>MRP<br/>1</b> | <b>MRP<br/>2</b> | <b>MRP<br/>3</b> | <b>MRP<br/>4</b> | <b>BCRP<br/>1</b>            | <b>Pgp</b>                                                                                                                                                  | <b>Zusatz</b>                                                                                                     | <b>Wechsel-<br/>wirkungen</b>                                                                   |
| Halofantrin                               | 8                         |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   | Quinin <sup>1</sup> <sub>t</sub>                                                                |
| Haloperidol                               | 16                        |                                         | MDR, MRP <sup>1</sup> <sub>vt</sub>                            | X <sup>2</sup> <sub>vt</sub> |                  |                  |                  |                  |                              | X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>r</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub> | kein Substrat <sup>7</sup> <sub>vt</sub>                                                                          |                                                                                                 |
| Halothan                                  | 3                         |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
| Hexobarbital                              | 1                         |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
| Hydralazin                                | 1                         |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
| Hydrocodon                                | 0                         |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
| Hydrocortison<br>-siehe Cortisol-         |                           |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
| Hydroxyzin                                | 10                        |                                         |                                                                |                              |                  |                  |                  |                  |                              | X <sup>1</sup> <sub>vt</sub>                                                                                                                                |                                                                                                                   |                                                                                                 |
| Hyperforin<br>(Johanniskraut)             | 20                        | MDR <sup>1</sup> <sub>vt</sub>          | Pgp <sup>2</sup> <sub>r</sub><br>Pgp <sup>3</sup> <sub>r</sub> |                              |                  |                  |                  |                  |                              | X <sup>4</sup> <sub>vt</sub>                                                                                                                                |                                                                                                                   | Ciclosporin,<br>Indinavir, Di-<br>goxin, Amitrip-<br>tylin <sup>5</sup> <sub>h</sub> <b>cop</b> |
| <b>Substanz</b>                           | <b>Anzahl<br/>Artikel</b> | <b>Wirkung auf<br/>Funktion<br/>von</b> | <b>Wirkung auf<br/>Expression<br/>von</b>                      | <b>MDR-<br/>Umkehr</b>       | <b>MRP<br/>1</b> | <b>MRP<br/>2</b> | <b>MRP<br/>3</b> | <b>MRP<br/>4</b> | <b>BCRP<br/>1</b>            | <b>Pgp</b>                                                                                                                                                  | <b>Zusatz</b>                                                                                                     | <b>Wechsel-<br/>wirkungen</b>                                                                   |
| Ibuprofen                                 | 12                        |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
| Ifosfamid                                 | 31                        |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |
| Imatinib                                  |                           |                                         |                                                                |                              |                  |                  |                  |                  |                              |                                                                                                                                                             |                                                                                                                   |                                                                                                 |

|                          |     |                                                                 |                                                                                                                                                                           |                              |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            |                                                                                                                                                                                              |  |                                                                                                                                                                                                                              |
|--------------------------|-----|-----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|--|------------------------------|--------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| -siehe Gleevec-          |     |                                                                 |                                                                                                                                                                           |                              |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            |                                                                                                                                                                                              |  |                                                                                                                                                                                                                              |
| Imipramin                | 29  |                                                                 |                                                                                                                                                                           |                              |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            | X <sup>1</sup> <sub>r</sub>                                                                                                                                                                  |  |                                                                                                                                                                                                                              |
| Imiquimod                | 2   |                                                                 |                                                                                                                                                                           |                              |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            |                                                                                                                                                                                              |  |                                                                                                                                                                                                                              |
| Indinavir                | 91  |                                                                 | Pgp <sup>1</sup> <sub>vt</sub>                                                                                                                                            |                              | X <sup>2</sup> <sub>vt</sub>                                                                                                                                                                                                                                 |                                                              |  |                              |                                                                                            | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub> |  | St John`s wort <sup>8</sup> <sub>cop</sub> , <sup>9</sup> <sub>r</sub> , <sup>10</sup> <sub>r</sub> ,<br><sup>11</sup> <sub>r</sub><br>Chloroquin <sup>12</sup> <sub>vt</sub><br>Grapefruit-saft <sup>13</sup> <sub>vt</sub> |
| Indomethacin             | 107 |                                                                 |                                                                                                                                                                           |                              | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub> |                                                              |  |                              |                                                                                            | X <sup>9</sup> <sub>vt</sub>                                                                                                                                                                 |  |                                                                                                                                                                                                                              |
| Indoramin                | 0   |                                                                 |                                                                                                                                                                           |                              |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            |                                                                                                                                                                                              |  |                                                                                                                                                                                                                              |
| Insulin                  | 422 |                                                                 |                                                                                                                                                                           |                              |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            | X <sup>1</sup> <sub>r</sub>                                                                                                                                                                  |  |                                                                                                                                                                                                                              |
| Interferon               | 569 | Pgp <sup>1</sup> <sub>r</sub><br>Pgp <sup>2</sup> <sub>vt</sub> | Pgp <sup>1</sup> <sub>r</sub><br>Pgp <sup>2</sup> <sub>vt</sub><br>Pgp <sup>3</sup> <sub>t</sub><br>MDR1/Pgp <sup>4</sup> <sub>vt</sub><br>Pgp <sup>5</sup> <sub>vt</sub> | X <sup>6</sup> <sub>vt</sub> |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            |                                                                                                                                                                                              |  |                                                                                                                                                                                                                              |
| Irbesartan               | 0   |                                                                 |                                                                                                                                                                           |                              |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            |                                                                                                                                                                                              |  |                                                                                                                                                                                                                              |
| Irinotecan               | 84  |                                                                 | Pgp <sup>1</sup> <sub>vt</sub>                                                                                                                                            |                              | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub>                                                                                                                                                                                                 | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub> |  | X <sup>2</sup> <sub>vt</sub> | X <sup>2</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>r</sub><br>X <sup>5</sup> <sub>r</sub> | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>r</sub><br>X <sup>5</sup> <sub>r</sub>                                                                   |  | St John`s wort <sup>6</sup> <sub>r</sub><br>cop                                                                                                                                                                              |
| Isofluran                | 9   |                                                                 |                                                                                                                                                                           |                              |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            |                                                                                                                                                                                              |  |                                                                                                                                                                                                                              |
| Isoniazid                | 10  |                                                                 |                                                                                                                                                                           |                              |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                 |  |                                                                                                                                                                                                                              |
| Isosorbiddinitrat (ISDN) | 1   |                                                                 |                                                                                                                                                                           |                              |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            |                                                                                                                                                                                              |  |                                                                                                                                                                                                                              |
| Isosorbid-mononitrat     | 0   |                                                                 |                                                                                                                                                                           |                              |                                                                                                                                                                                                                                                              |                                                              |  |                              |                                                                                            |                                                                                                                                                                                              |  |                                                                                                                                                                                                                              |

|                                     |                       |                                 |                                   |                   |                              |              |              |              |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                           |                                                                                                                                                                                                                                               |
|-------------------------------------|-----------------------|---------------------------------|-----------------------------------|-------------------|------------------------------|--------------|--------------|--------------|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| (ISMN)                              |                       |                                 |                                   |                   |                              |              |              |              |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                           |                                                                                                                                                                                                                                               |
| Isradipin                           | 4                     |                                 |                                   |                   |                              |              |              |              |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                           |                                                                                                                                                                                                                                               |
| Itraconazol                         | 70                    |                                 |                                   |                   |                              |              |              |              |               | <del>X</del> <sup>1</sup> <sub>h</sub><br><del>X</del> <sup>2</sup> <sub>r</sub><br><del>X</del> <sup>3</sup> <sub>vt</sub><br><del>X</del> <sup>4</sup> <sub>h</sub><br><del>X</del> <sup>5</sup> <sub>vt</sub><br><del>X</del> <sup>6</sup> <sub>h</sub><br><del>X</del> <sup>7</sup> <sub>h</sub><br><del>X</del> <sup>8</sup> <sub>t</sub>                                                                                                                                                                                 | Bezieht sich auf OH-Itraconazol <sup>9</sup> <sub>h</sub> | Cyclosporin A <sup>9</sup> <sub>h</sub>                                                                                                                                                                                                       |
| Ivermectin                          | 75                    |                                 |                                   |                   | X <sup>1</sup> <sub>vt</sub> |              |              |              |               | <del>X</del> <sup>1</sup> <sub>vt</sub><br><del>X</del> <sup>2</sup> <sub>vt</sub><br><del>X</del> <sup>3</sup> <sub>vt</sub><br><del>X</del> <sup>4</sup> <sub>r</sub><br><del>X</del> <sup>5</sup> <sub>t</sub><br><del>X</del> <sup>6</sup> <sub>vt</sub><br><del>X</del> <sup>7</sup> <sub>t</sub><br><del>X</del> <sup>8</sup> <sub>vt</sub><br><del>X</del> <sup>9</sup> <sub>t</sub><br><del>X</del> <sup>10</sup> <sub>t</sub><br><del>X</del> <sup>11</sup> <sub>vt</sub><br><del>X</del> <sup>12</sup> <sub>vt</sub> |                                                           | Loperamid <sup>9</sup> <sub>t</sub><br>Verapamil <sup>13</sup> <sub>t</sub><br>Itraconazol <sup>14</sup> <sub>t</sub> ,<br><sup>15</sup> <sub>t</sub><br>Oxytetracyclin <sup>16</sup> <sub>vt</sub><br>Ketaconazol <sup>17</sup> <sub>t</sub> |
|                                     |                       |                                 |                                   |                   |                              |              |              |              |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                           |                                                                                                                                                                                                                                               |
| <b>Substanz</b>                     | <b>Anzahl Artikel</b> | <b>Wirkung auf Funktion von</b> | <b>Wirkung auf Expression von</b> | <b>MDR-Umkehr</b> | <b>MRP 1</b>                 | <b>MRP 2</b> | <b>MRP 3</b> | <b>MRP 4</b> | <b>BCRP 1</b> | <b>Pgp</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <b>Zusatz</b>                                             | <b>Wechselwirkungen</b>                                                                                                                                                                                                                       |
| Johanniskraut<br>-siehe Hyperforin- |                       |                                 |                                   |                   |                              |              |              |              |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                           |                                                                                                                                                                                                                                               |
| Josamycin                           | 3                     |                                 |                                   |                   |                              |              |              |              |               | <del>X</del> <sup>1</sup> <sub>h</sub><br><del>X</del> <sup>2</sup> <sub>h</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                           |                                                                                                                                                                                                                                               |
| Ketamin                             | 4                     |                                 |                                   |                   |                              |              |              |              |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                           | Cyclosporin <sup>1</sup> <sub>t</sub>                                                                                                                                                                                                         |
| Ketoconazol                         | 39                    |                                 |                                   |                   |                              |              |              |              |               | <del>X</del> <sup>1</sup> <sub>vt</sub><br><del>X</del> <sup>2</sup> <sub>vt</sub><br><del>X</del> <sup>3</sup> <sub>t</sub>                                                                                                                                                                                                                                                                                                                                                                                                   |                                                           | Epigallocatechin-3-gallate, Xantho-                                                                                                                                                                                                           |

|                                    |                       |                                 |                                   |                   |                              |                              |                              |              |               |                                                                                                                                                                                                                                                              |               |                                          |
|------------------------------------|-----------------------|---------------------------------|-----------------------------------|-------------------|------------------------------|------------------------------|------------------------------|--------------|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|------------------------------------------|
|                                    |                       |                                 |                                   |                   |                              |                              |                              |              |               | X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>t</sub><br>X <sup>9</sup> <sub>h</sub><br>X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>vt</sub> |               | humol <sup>11</sup> <sub>vt</sub>        |
| Ketoprofen                         | 6                     |                                 |                                   |                   |                              |                              |                              |              |               |                                                                                                                                                                                                                                                              |               |                                          |
| <b>Substanz</b>                    | <b>Anzahl Artikel</b> | <b>Wirkung auf Funktion von</b> | <b>Wirkung auf Expression von</b> | <b>MDR-Umkehr</b> | <b>MRP 1</b>                 | <b>MRP 2</b>                 | <b>MRP 3</b>                 | <b>MRP 4</b> | <b>BCRP 1</b> | <b>Pgp</b>                                                                                                                                                                                                                                                   | <b>Zusatz</b> | <b>Wechselwirkungen</b>                  |
| LAAM (Levacetyl-methadol)          | 2                     |                                 |                                   |                   |                              |                              |                              |              |               | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub>                                                                                                                                                                                                 |               |                                          |
| Labetalol                          | 2                     |                                 |                                   |                   |                              |                              |                              |              |               | X <sup>1</sup> <sub>t</sub>                                                                                                                                                                                                                                  |               |                                          |
| Lamivudin                          | 15                    |                                 |                                   |                   | X <sup>1</sup> <sub>vt</sub> | X <sup>1</sup> <sub>vt</sub> | X <sup>1</sup> <sub>vt</sub> |              |               |                                                                                                                                                                                                                                                              |               |                                          |
| Lamotrigin                         | 9                     |                                 |                                   |                   |                              |                              |                              |              |               | X <sup>1</sup> <sub>t</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>r</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub>                                                                    |               |                                          |
| Lansoprazol                        | 7                     |                                 |                                   |                   |                              |                              |                              |              |               | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>h</sub>                                                                                                                                                                                                  |               | Clarithromycin <sup>3</sup> <sub>h</sub> |
| Leflunomid                         | 1                     |                                 |                                   |                   |                              |                              |                              |              |               |                                                                                                                                                                                                                                                              |               |                                          |
| Lercanidipin                       | 1                     |                                 |                                   |                   |                              |                              |                              |              |               |                                                                                                                                                                                                                                                              |               |                                          |
| Letrozol                           | 1                     |                                 |                                   |                   |                              |                              |                              |              |               |                                                                                                                                                                                                                                                              |               | Tamoxifen <sup>1</sup> <sub>r</sub>      |
| Levacetyl-methadol<br>-siehe LAAM- |                       |                                 |                                   |                   |                              |                              |                              |              |               |                                                                                                                                                                                                                                                              |               |                                          |
| Levofloxacin                       | 23                    |                                 | Pgp <sup>1</sup> <sub>vt</sub>    |                   | X <sup>2</sup> <sub>vt</sub> |                              |                              |              |               | X <sup>3</sup> <sub>t</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub>                                                                                                                                  |               | Orangensaft <sup>10</sup> <sub>h</sub>   |



|                      |    |                                |                                |                              |                              |                                                              |  |  |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |                                                                                                                                                   |
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|                      |    |                                |                                |                              |                              |                                                              |  |  |                                       | X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>t</sub><br><del>X<sup>9</sup><sub>vt</sub></del>                                                                                                                                                                                                                                                                                                                                                                                      |  |                                                                                                                                                   |
| Levomopromazin       | 3  |                                |                                |                              |                              |                                                              |  |  |                                       | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |                                                                                                                                                   |
| Levonorgestrel       | 7  |                                |                                |                              |                              |                                                              |  |  |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |                                                                                                                                                   |
| Levothyroxin-Natrium | 0  |                                |                                |                              |                              |                                                              |  |  |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |                                                                                                                                                   |
| Lidocain             | 11 |                                |                                | X <sup>1</sup> <sub>vt</sub> |                              |                                                              |  |  |                                       | <del>X<sup>2</sup><sub>vt</sub></del>                                                                                                                                                                                                                                                                                                                                                                                                                                                     |  |                                                                                                                                                   |
| Lomefloxacin         | 2  |                                |                                |                              |                              |                                                              |  |  |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |                                                                                                                                                   |
| Lomustin             | 5  |                                |                                |                              |                              |                                                              |  |  |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |                                                                                                                                                   |
| Loperamid            | 46 |                                |                                |                              |                              |                                                              |  |  |                                       | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>h</sub><br>X <sup>3</sup> <sub>t</sub><br>X <sup>4</sup> <sub>t</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>t</sub><br>X <sup>9</sup> <sub>h</sub><br>X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>r</sub><br>X <sup>12</sup> <sub>r</sub><br>X <sup>13</sup> <sub>t</sub><br>X <sup>14</sup> <sub>t</sub><br>X <sup>15</sup> <sub>vt</sub> |  | Quinidin <sup>15</sup> <sub>vt</sub><br>Tipranavir <sup>16</sup> <sub>h</sub><br>Itraconazol,<br>Gemfibrozil <sup>17</sup> <sub>h</sub>           |
| Lopinavir            | 20 |                                | Pgp <sup>1</sup> <sub>vt</sub> |                              | X <sup>2</sup> <sub>vt</sub> | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub> |  |  | <del>X<sup>4</sup><sub>vt</sub></del> | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br><del>X<sup>5</sup><sub>vt</sub></del><br><del>X<sup>6</sup><sub>vt</sub></del><br><del>X<sup>7</sup><sub>vt</sub></del>                                                                                                                                                                                                                                                                                                   |  | Ritonavir, Amprenavir, Atazanavir <sup>2</sup> <sub>vt</sub><br>St John`s wort <sup>8</sup> <sub>r</sub><br>Fexofenadin <sup>9</sup> <sub>h</sub> |
| Loratadin            | 8  | Pgp <sup>1</sup> <sub>vt</sub> |                                |                              |                              |                                                              |  |  |                                       | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                                              |  |                                                                                                                                                   |
| Losartan             | 11 |                                |                                |                              |                              |                                                              |  |  |                                       | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  | Grapefruit-                                                                                                                                       |

|                           |                       |                                 |                                   |                                                              |              |              |              |              |               |                                                                                                                                                                                               |                                                                                                                                                                     |                                                                                      |
|---------------------------|-----------------------|---------------------------------|-----------------------------------|--------------------------------------------------------------|--------------|--------------|--------------|--------------|---------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
|                           |                       |                                 |                                   |                                                              |              |              |              |              |               | X <sup>2</sup> <sub>vt</sub>                                                                                                                                                                  |                                                                                                                                                                     | Saft <sup>3</sup> <sub>h</sub> , <sup>4</sup> <sub>r</sub>                           |
| Lovastatin                | 32                    |                                 | Pgp <sup>1</sup> <sub>vt</sub>    |                                                              |              |              |              |              |               | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>r</sub>                                   | Interaktion mit MDR 1 <sup>7</sup> <sub>vt</sub><br>Lakton-Form ist MDR1-Inhibitor <sup>8</sup> <sub>vt</sub><br>Lakton-Form ist Substrat <sup>9</sup> <sub>t</sub> | Cyclosporin <sup>10</sup> <sub>r</sub><br>Grapefruit-Saft <sup>11</sup> <sub>r</sub> |
| Lumiracoxib               | 0                     |                                 |                                   |                                                              |              |              |              |              |               |                                                                                                                                                                                               |                                                                                                                                                                     |                                                                                      |
| <b>Substanz</b>           | <b>Anzahl Artikel</b> | <b>Wirkung auf Funktion von</b> | <b>Wirkung auf Expression von</b> | <b>MDR-Umkehr</b>                                            | <b>MRP 1</b> | <b>MRP 2</b> | <b>MRP 3</b> | <b>MRP 4</b> | <b>BCRP 1</b> | <b>Pgp</b>                                                                                                                                                                                    | <b>Zusatz</b>                                                                                                                                                       | <b>Wechselwirkungen</b>                                                              |
| Maprotilin                | 0                     |                                 |                                   |                                                              |              |              |              |              |               |                                                                                                                                                                                               |                                                                                                                                                                     |                                                                                      |
| MDMA<br>-siehe "Ecstasy"- |                       |                                 |                                   |                                                              |              |              |              |              |               |                                                                                                                                                                                               |                                                                                                                                                                     |                                                                                      |
| Medroxy-progesteron       | 13                    |                                 |                                   | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> |              |              |              |              |               | X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub>                                                                                                                                  |                                                                                                                                                                     |                                                                                      |
| Mefenaminsäure            | 1                     |                                 |                                   |                                                              |              |              |              |              |               |                                                                                                                                                                                               |                                                                                                                                                                     |                                                                                      |
| Mefloquin                 | 38                    |                                 | Pgp <sup>1</sup> <sub>vt</sub>    |                                                              |              |              |              |              |               | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>XX <sup>5</sup> <sub>vt</sub><br>XX <sup>6</sup> <sub>t</sub> |                                                                                                                                                                     | Fluoxetin <sup>7</sup> <sub>vt</sub><br>Roxythromycin <sup>8</sup> <sub>vt</sub>     |
| Melatonin                 | 1                     |                                 |                                   |                                                              |              |              |              |              |               |                                                                                                                                                                                               |                                                                                                                                                                     | Doxoubicin <sup>1</sup> <sub>vt</sub>                                                |
| Meloxicam                 | 2                     |                                 |                                   |                                                              |              |              |              |              |               |                                                                                                                                                                                               | mdr1b-mRNA-Expression-Inhibitor <sup>1</sup> <sub>vt</sub>                                                                                                          |                                                                                      |
| Melperon                  | 1                     |                                 |                                   |                                                              |              |              |              |              |               |                                                                                                                                                                                               |                                                                                                                                                                     |                                                                                      |
| Mephenytoin               | 9                     |                                 |                                   |                                                              |              |              |              |              |               |                                                                                                                                                                                               |                                                                                                                                                                     |                                                                                      |
| Mestranol                 | 1                     |                                 |                                   |                                                              |              |              |              |              |               |                                                                                                                                                                                               |                                                                                                                                                                     |                                                                                      |
| Metformin                 | 2                     |                                 |                                   |                                                              |              |              |              |              |               |                                                                                                                                                                                               |                                                                                                                                                                     |                                                                                      |
| Methamphetamine           | 3                     |                                 |                                   |                                                              |              |              |              |              |               | X <sup>1</sup> <sub>t</sub>                                                                                                                                                                   |                                                                                                                                                                     |                                                                                      |
| Methadon                  | 36                    |                                 |                                   |                                                              |              |              |              |              |               | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>t</sub>                                                                                                   | L-alpha-acetyl-methadol (LAAM) = Substrat <sup>12</sup> <sub>vt</sub>                                                                                               | Rifampicin <sup>13</sup> <sub>r</sub><br>St John's wort <sup>14</sup> <sub>r</sub>   |

|                          |    |  |  |            |  |  |  |  |  |                                                                                                     |                                      |                                                                                |
|--------------------------|----|--|--|------------|--|--|--|--|--|-----------------------------------------------------------------------------------------------------|--------------------------------------|--------------------------------------------------------------------------------|
|                          |    |  |  |            |  |  |  |  |  | $X_t^4$<br>$X_h^5$<br>$X_{vt}^6$<br>$X_{vt}^7$<br>$X_t^8$<br>$X_{vt}^9$<br>$X_r^{10}$<br>$X_h^{11}$ |                                      |                                                                                |
| Methosuximid             | 0  |  |  |            |  |  |  |  |  |                                                                                                     |                                      |                                                                                |
| Methoxsalen              | 3  |  |  |            |  |  |  |  |  |                                                                                                     |                                      |                                                                                |
| Methoxy-<br>amphetamin   | 1  |  |  |            |  |  |  |  |  |                                                                                                     |                                      |                                                                                |
| Methoxyfluran            | 0  |  |  |            |  |  |  |  |  |                                                                                                     |                                      |                                                                                |
| Methylphenidat           | 2  |  |  |            |  |  |  |  |  | $X_t^1$<br>$X_{vt}^2$                                                                               |                                      |                                                                                |
| Methylpheno-<br>barbital | 0  |  |  |            |  |  |  |  |  |                                                                                                     |                                      |                                                                                |
| Methylpred-<br>nisolon   | 21 |  |  |            |  |  |  |  |  | $X_t^1$<br>$X_t^2$<br>$X_{vt}^3$<br>$X_{vt}^4$<br>$X_{vt}^5$<br>$X_t^6$                             |                                      | Cyclosporin A <sup>7</sup> <sub>t</sub><br>Verapamil <sup>8</sup> <sub>t</sub> |
| Methysergid              | 0  |  |  |            |  |  |  |  |  |                                                                                                     |                                      |                                                                                |
| Metoclopramid            | 0  |  |  |            |  |  |  |  |  |                                                                                                     |                                      |                                                                                |
| Metoprolol               | 15 |  |  |            |  |  |  |  |  |                                                                                                     | Modulator <sup>1</sup> <sub>vt</sub> |                                                                                |
| Metronidazol             | 10 |  |  |            |  |  |  |  |  |                                                                                                     |                                      | Silymarin <sup>1</sup> <sub>h</sub>                                            |
| Mexiletin                | 1  |  |  |            |  |  |  |  |  |                                                                                                     |                                      |                                                                                |
| Mianserin                | 2  |  |  |            |  |  |  |  |  | $X_{vt}^1$                                                                                          |                                      |                                                                                |
| Mibefradil               | 2  |  |  |            |  |  |  |  |  | $X_{vt}^1$                                                                                          |                                      |                                                                                |
| Miconazol                | 6  |  |  |            |  |  |  |  |  | $X_{vt}^1$                                                                                          |                                      |                                                                                |
| Midazolam                | 75 |  |  |            |  |  |  |  |  |                                                                                                     |                                      |                                                                                |
| Mifepriston              | 20 |  |  | $X_{vt}^1$ |  |  |  |  |  | $X_{vt}^2$                                                                                          |                                      |                                                                                |

|             |     |                               |  |  |                                                              |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                       |                                                                         |                                                                                                                                                                                                                                                                                                          |
|-------------|-----|-------------------------------|--|--|--------------------------------------------------------------|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|             |     |                               |  |  |                                                              |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                             | X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>r</sub><br>X <sup>8</sup> <sub>vt</sub>                                                                                                                           |                                                                         |                                                                                                                                                                                                                                                                                                          |
| Minaprin    | 0   |                               |  |  |                                                              |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                       |                                                                         |                                                                                                                                                                                                                                                                                                          |
| Mirtazapin  | 2   |                               |  |  |                                                              |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                       |                                                                         |                                                                                                                                                                                                                                                                                                          |
| Mitoxantron | 233 |                               |  |  | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> |  |  |  | X <sup>1</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>t</sub><br>X <sup>6</sup> <sub>r</sub><br>X <sup>7</sup> <sub>h</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>r</sub><br>X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>r</sub><br>X <sup>12</sup> <sub>vt</sub><br>X <sup>13</sup> <sub>vt</sub> | X <sup>1</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>vt</sub>                                                                                                                                                                                                                                                         | Eigenes ABC-Gen-<br>Produkt: MXR<br>(=ABCG2) <sup>14</sup> <sub>r</sub> | Cyclosporin,<br>PSC-833 <sup>1</sup> <sub>vt</sub><br>Cannaboids <sup>13</sup> <sub>vt</sub><br>Tetrahydro-<br>curcumin<br>(THC) <sup>15</sup> <sub>vt</sub><br>Gefitinib, Er-<br>lotinib <sup>16</sup> <sub>vt</sub><br>Zosuquidar <sup>17</sup> <sub>vt</sub><br>Chalcones <sup>18</sup> <sub>vt</sub> |
| Moclobemid  | 2   |                               |  |  |                                                              |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                       |                                                                         |                                                                                                                                                                                                                                                                                                          |
| Modafinil   | 1   |                               |  |  |                                                              |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                             | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                          |                                                                         | PSC-833 <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                       |
| Montelukast | 0   |                               |  |  |                                                              |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                       |                                                                         |                                                                                                                                                                                                                                                                                                          |
| Moricizin   | 0   |                               |  |  |                                                              |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                       |                                                                         |                                                                                                                                                                                                                                                                                                          |
| Morphin     | 66  | Pgp <sup>1</sup> <sub>t</sub> |  |  |                                                              |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                             | X <sup>1</sup> <sub>t</sub><br>X <sup>2</sup> <sub>h</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>t</sub><br>X <sup>5</sup> <sub>t</sub><br>X <sup>6</sup> <sub>r</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>t</sub><br>X <sup>9</sup> <sub>h</sub><br>X <sup>10</sup> <sub>r</sub> |                                                                         | Quinidin <sup>2</sup> <sub>h</sub>                                                                                                                                                                                                                                                                       |

| Substanz                | Anzahl Artikel | Wirkung auf Funktion von                                               | Wirkung auf Expression von                                       | MDR-Umkehr                                                                                                                                                  | MRP 1                                                       | MRP 2                        | MRP 3                        | MRP 4 | BCRP 1                                                                                                                      | Pgp                                                                                                                                                                                                                                                                                         | Zusatz | Wechselwirkungen                                     |
|-------------------------|----------------|------------------------------------------------------------------------|------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|------------------------------|------------------------------|-------|-----------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|------------------------------------------------------|
| Nafcillin               | 1              |                                                                        |                                                                  |                                                                                                                                                             |                                                             |                              |                              |       |                                                                                                                             | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                |        |                                                      |
| Nalidixinsäure          | 0              |                                                                        |                                                                  |                                                                                                                                                             |                                                             |                              |                              |       |                                                                                                                             |                                                                                                                                                                                                                                                                                             |        |                                                      |
| Naphtoflavon            | 10             |                                                                        | MDR1 <sup>1</sup> <sub>vt</sub>                                  |                                                                                                                                                             |                                                             |                              |                              |       |                                                                                                                             |                                                                                                                                                                                                                                                                                             |        |                                                      |
| Naproxen                | 4              |                                                                        | Pgp <sup>1</sup> <sub>vt</sub>                                   |                                                                                                                                                             |                                                             |                              |                              |       |                                                                                                                             |                                                                                                                                                                                                                                                                                             |        |                                                      |
| Naringenin (Grapefruit) | 22             |                                                                        | Pgp <sup>1</sup> <sub>vt</sub>                                   |                                                                                                                                                             |                                                             |                              |                              |       | X <sup>2</sup> <sub>vt</sub>                                                                                                | X <sup>1</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>t</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>t</sub> |        | 30 Medikamente <sup>11</sup> <sub>r</sub>            |
| Nateglinid              | 0              |                                                                        |                                                                  |                                                                                                                                                             |                                                             |                              |                              |       |                                                                                                                             |                                                                                                                                                                                                                                                                                             |        |                                                      |
| Nefazodon               | 4              |                                                                        | Pgp <sup>1</sup> <sub>vt</sub>                                   |                                                                                                                                                             |                                                             |                              |                              |       |                                                                                                                             | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                |        | St John`s wort <sup>2</sup> <sub>r</sub>             |
| Nelfinavir              | 54             |                                                                        | Pgp <sup>1</sup> <sub>vt</sub><br>Pgp <sup>2</sup> <sub>vt</sub> |                                                                                                                                                             | X <sup>3</sup> <sub>r</sub><br>X <sup>1</sup> <sub>vt</sub> | X <sup>3</sup> <sub>r</sub>  |                              |       | X <sup>3</sup> <sub>r</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub> | X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>h</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>r</sub><br>X <sup>11</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>t</sub><br>X <sup>13</sup> <sub>r</sub>                                 |        |                                                      |
| Nevirapin               | 19             | Pgp <sup>1</sup> <sub>vt</sub>                                         | Pgp <sup>1</sup> <sub>vt</sub>                                   |                                                                                                                                                             | X <sup>2</sup> <sub>tv</sub>                                | X <sup>2</sup> <sub>vt</sub> | X <sup>2</sup> <sub>vt</sub> |       | X <sup>3</sup> <sub>vt</sub>                                                                                                | X <sup>4</sup> <sub>h</sub><br>X <sup>5</sup> <sub>h</sub><br>X <sup>6</sup> <sub>vt</sub>                                                                                                                                                                                                  |        | St John`s wort <sup>7, 8, 9</sup> <sub>r, r, r</sub> |
| Nicardipin              | 49             | ATPase <sup>1</sup> <sub>vt</sub><br>ATPase <sup>2</sup> <sub>vt</sub> | mdr1-mRNA <sup>3</sup> <sub>vt</sub>                             | X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>h</sub><br>X <sup>8</sup> <sub>vt</sub> |                                                             |                              |                              |       | X <sup>9</sup> <sub>vt</sub>                                                                                                | X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>vt</sub><br>X <sup>13</sup> <sub>vt</sub><br>X <sup>14</sup> <sub>vt</sub>                                                                                                                           |        | Grapefruit-Saft <sup>19</sup> <sub>r</sub>           |

|                   |    |                                 |                                                                                                                                   |                                                                                                                              |  |  |  |  |                              |                                                                                                                                  |                                         |                                                                                                                                                                                                                                                            |
|-------------------|----|---------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|------------------------------|----------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                   |    |                                 |                                                                                                                                   |                                                                                                                              |  |  |  |  |                              | X <sup>15</sup> <sub>vt</sub><br>X <sup>16</sup> <sub>vt</sub><br>X <sup>17</sup> <sub>vt</sub><br>X <sup>18</sup> <sub>vt</sub> |                                         |                                                                                                                                                                                                                                                            |
| Nikotin („smoke“) | 13 | MDR1 <sup>1</sup> <sub>vt</sub> | Pgp <sup>2</sup> <sub>t</sub><br>Pgp <sup>3</sup> <sub>t</sub><br>MRP1 <sup>4</sup> <sub>h</sub><br>Pgp <sup>5</sup> <sub>h</sub> |                                                                                                                              |  |  |  |  |                              |                                                                                                                                  |                                         |                                                                                                                                                                                                                                                            |
| Trp-P-2           |    |                                 |                                                                                                                                   |                                                                                                                              |  |  |  |  |                              |                                                                                                                                  | 3-amino-1-methyl-5H-pyrido[4,3-b]indole | Trifluoperazin <sup>6</sup> <sub>vt</sub>                                                                                                                                                                                                                  |
| Nifedipin         | 76 |                                 |                                                                                                                                   |                                                                                                                              |  |  |  |  |                              | X <sup>1</sup> <sub>r</sub>                                                                                                      |                                         | Grapefruit-Saft <sup>2</sup> <sub>r</sub><br>Rifampin <sup>3</sup> <sub>r</sub><br>St John`s wort <sup>4</sup> <sub>r</sub>                                                                                                                                |
| Nilutamid         | 0  |                                 |                                                                                                                                   |                                                                                                                              |  |  |  |  |                              |                                                                                                                                  |                                         |                                                                                                                                                                                                                                                            |
| Nimodipin         | 25 |                                 |                                                                                                                                   | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub> |  |  |  |  |                              | X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub>                                     |                                         | Cyclosporin A <sup>8</sup> <sub>t</sub><br>Grapefruit-Saft <sup>9</sup> <sub>r</sub><br>Morin <sup>10</sup> <sub>t</sub><br>Huang-Lian-Jie-Du-Tang (HLJDT) <sup>11</sup> <sub>t, vt</sub><br>Erythromycin, Clarithromycin, CsA <sup>12</sup> <sub>vt</sub> |
| Nisoldipin        | 1  |                                 |                                                                                                                                   |                                                                                                                              |  |  |  |  |                              |                                                                                                                                  |                                         | Grapefruit-Saft <sup>1</sup> <sub>r</sub>                                                                                                                                                                                                                  |
| Nitrazepam        | 0  |                                 |                                                                                                                                   |                                                                                                                              |  |  |  |  |                              |                                                                                                                                  |                                         |                                                                                                                                                                                                                                                            |
| Nitrendipin       | 13 |                                 |                                                                                                                                   | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub>                                                                 |  |  |  |  | X <sup>3</sup> <sub>vt</sub> | X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>r</sub><br>X <sup>6</sup> <sub>t</sub><br>X <sup>7</sup> <sub>vt</sub>       |                                         | Grapefruit-Saft <sup>8</sup> <sub>r</sub>                                                                                                                                                                                                                  |
| Nordazepam        | 0  |                                 |                                                                                                                                   |                                                                                                                              |  |  |  |  |                              |                                                                                                                                  |                                         |                                                                                                                                                                                                                                                            |
| Norethindron      | 2  |                                 |                                                                                                                                   |                                                                                                                              |  |  |  |  |                              |                                                                                                                                  |                                         |                                                                                                                                                                                                                                                            |
| Norethisteron     | 4  |                                 |                                                                                                                                   |                                                                                                                              |  |  |  |  |                              |                                                                                                                                  |                                         |                                                                                                                                                                                                                                                            |
| Norfloxacin       | 9  |                                 |                                                                                                                                   |                                                                                                                              |  |  |  |  |                              |                                                                                                                                  |                                         |                                                                                                                                                                                                                                                            |

|                                |                       |                                          |                                   |                   |                                                              |              |              |              |                              |                                                                                                                                                         |               |                                                                                                                       |
|--------------------------------|-----------------------|------------------------------------------|-----------------------------------|-------------------|--------------------------------------------------------------|--------------|--------------|--------------|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|-----------------------------------------------------------------------------------------------------------------------|
| Norfluoxetin                   | 1                     |                                          |                                   |                   |                                                              |              |              |              |                              | X <sup>1</sup> <sub>vt</sub>                                                                                                                            |               |                                                                                                                       |
| Nortriptylin                   | 8                     |                                          |                                   |                   |                                                              |              |              |              |                              | X <sup>1</sup> <sub>h</sub><br>X <sup>2</sup> <sub>t</sub><br>X <sup>3</sup> <sub>t</sub><br>X <sup>4</sup> <sub>t</sub><br>X <sup>5</sup> <sub>t</sub> |               | St John`s wort <sup>6</sup> <sub>vt</sub>                                                                             |
| N-Propylajmalin                | 0                     |                                          |                                   |                   |                                                              |              |              |              |                              |                                                                                                                                                         |               |                                                                                                                       |
| <b>Substanz</b>                | <b>Anzahl Artikel</b> | <b>Wirkung auf Funktion von</b>          | <b>Wirkung auf Expression von</b> | <b>MDR-Umkehr</b> | <b>MRP 1</b>                                                 | <b>MRP 2</b> | <b>MRP 3</b> | <b>MRP 4</b> | <b>BCRP 1</b>                | <b>Pgp</b>                                                                                                                                              | <b>Zusatz</b> | <b>Wechselwirkungen</b>                                                                                               |
| Ondanestron                    | 9                     |                                          |                                   |                   |                                                              |              |              |              |                              | X <sup>1</sup> <sub>t</sub><br>X <sup>2</sup> <sub>t</sub><br>X <sup>3</sup> <sub>t</sub>                                                               |               |                                                                                                                       |
| Ofloxacin                      | 17                    |                                          |                                   |                   | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub> |              |              |              | X <sup>3</sup> <sub>vt</sub> | X <sup>4</sup> <sub>t</sub><br>X <sup>5</sup> <sub>t</sub>                                                                                              |               | Quinidin, Ciprofloxacin <sup>6</sup> <sub>t</sub>                                                                     |
| Östradiol<br>-siehe Estradiol- |                       |                                          |                                   |                   |                                                              |              |              |              |                              |                                                                                                                                                         |               |                                                                                                                       |
| Olanzapin                      | 9                     | Pgp-Aktivität <sup>1</sup> <sub>vt</sub> |                                   |                   |                                                              |              |              |              |                              | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>t</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>t</sub>                              |               |                                                                                                                       |
| Omeprazol                      | 19                    |                                          |                                   |                   |                                                              |              |              |              |                              | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub>                                                                                            |               | Fluvoxamin <sup>3</sup> <sub>h</sub><br>Digoxin <sup>4</sup> <sub>h</sub><br>St John`s wort <sup>5</sup> <sub>r</sub> |
| Ondansetron                    | 9                     |                                          |                                   |                   |                                                              |              |              |              |                              | X <sup>1</sup> <sub>t</sub><br>X <sup>2</sup> <sub>t</sub><br>X <sup>3</sup> <sub>t</sub>                                                               |               | Rifampin <sup>4</sup> <sub>r</sub>                                                                                    |
| Orphenadrin                    | 0                     |                                          |                                   |                   |                                                              |              |              |              |                              |                                                                                                                                                         |               |                                                                                                                       |
| Oxazepam                       | 0                     |                                          |                                   |                   |                                                              |              |              |              |                              |                                                                                                                                                         |               |                                                                                                                       |
| Oxcarbazepin                   | 4                     |                                          |                                   |                   |                                                              |              |              |              |                              | X <sup>1</sup> <sub>t</sub><br>X <sup>2</sup> <sub>h</sub>                                                                                              |               |                                                                                                                       |
| Oxprenolol                     | 0                     |                                          |                                   |                   |                                                              |              |              |              |                              |                                                                                                                                                         |               |                                                                                                                       |
| Oxybutynin                     | 0                     |                                          |                                   |                   |                                                              |              |              |              |                              |                                                                                                                                                         |               |                                                                                                                       |
| Oxycodon                       | 3                     |                                          | Pgp <sup>1</sup> <sub>vt</sub>    |                   |                                                              |              |              |              |                              | X <sup>1</sup> <sub>vt</sub>                                                                                                                            |               |                                                                                                                       |

| Substanz           | Anzahl Artikel | Wirkung auf Funktion von                                              | Wirkung auf Expression von                                                                                                           | MDR-Umkehr                                                                                                                                                   | MRP 1 | MRP 2 | MRP 3 | MRP 4 | BCRP 1                                                                           | Pgp                                                                                                                                                                                                                                     | Zusatz | Wechselwirkungen                                                                                                                                                             |
|--------------------|----------------|-----------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|-------|-------|-------|----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Paclitaxel (Taxol) | 660            |                                                                       |                                                                                                                                      |                                                                                                                                                              |       |       |       |       |                                                                                  | X <sup>1</sup> <sub>r</sub><br>X <sup>2</sup> <sub>vt</sub>                                                                                                                                                                             |        | Edotecarin <sup>3</sup> <sub>r</sub><br>Glukokortikoid,<br>Trichostatin<br>A <sup>4</sup> <sub>vt</sub><br>Bexaroten <sup>5</sup> <sub>vt</sub> , <sup>6</sup> <sub>vt</sub> |
| Paliperidon        | 10             |                                                                       |                                                                                                                                      |                                                                                                                                                              |       |       |       |       |                                                                                  | X <sup>1</sup> <sub>t</sub><br>X <sup>2</sup> <sub>vt, t</sub><br><del>X<sup>3</sup><sub>vt</sub></del><br><del>X<sup>4</sup><sub>vt</sub></del><br>X <sup>5</sup> <sub>h</sub><br>X <sup>6</sup> <sub>t</sub>                          |        | Rifampin <sup>7</sup> <sub>h</sub>                                                                                                                                           |
| Pantoprazol        | 7              |                                                                       |                                                                                                                                      |                                                                                                                                                              |       |       |       |       | <del>X<sup>1</sup><sub>t, vt</sub></del><br><del>X<sup>2</sup><sub>t</sub></del> | <del>X<sup>1</sup><sub>t, vt</sub></del><br><del>X<sup>3</sup><sub>vt</sub></del>                                                                                                                                                       |        | Imatinib <sup>4</sup> <sub>t</sub>                                                                                                                                           |
| Paracetamol        | 13             | Pgp, Mrp2 <sup>1</sup> <sub>t</sub><br>Pgp <sup>2</sup> <sub>vt</sub> | Pgp, Mrp2 <sup>1</sup> <sub>t</sub><br>Pgp <sup>2</sup> <sub>vt</sub><br>MRP1, MRP4,<br>MRP5, BCRP<br>Pgp <sup>3</sup> <sub>vt</sub> |                                                                                                                                                              |       |       |       |       |                                                                                  | X <sup>2</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub>                                                                                                                                                                            |        |                                                                                                                                                                              |
| Parecoxib          | 0              |                                                                       |                                                                                                                                      |                                                                                                                                                              |       |       |       |       |                                                                                  |                                                                                                                                                                                                                                         |        |                                                                                                                                                                              |
| Paroxetin          | 14             |                                                                       |                                                                                                                                      |                                                                                                                                                              |       |       |       |       |                                                                                  | <del>X<sup>1</sup><sub>vt</sub></del><br><del>X<sup>2</sup><sub>t</sub></del><br><del>X<sup>3</sup><sub>vt</sub></del><br><del>X<sup>4</sup><sub>vt</sub></del><br><del>X<sup>5</sup><sub>vt</sub></del><br>X <sup>6</sup> <sub>h</sub> |        | Itraconazol <sup>6</sup> <sub>h</sub><br>St John`s<br>wort <sup>7</sup> <sub>r</sub> , <sup>8</sup> <sub>r</sub>                                                             |
| Penbutolol         | 0              |                                                                       |                                                                                                                                      |                                                                                                                                                              |       |       |       |       |                                                                                  |                                                                                                                                                                                                                                         |        |                                                                                                                                                                              |
| Pentamidin         | 5              |                                                                       |                                                                                                                                      |                                                                                                                                                              |       |       |       |       |                                                                                  |                                                                                                                                                                                                                                         |        |                                                                                                                                                                              |
| Pentobarbital      | 4              |                                                                       |                                                                                                                                      |                                                                                                                                                              |       |       |       |       |                                                                                  |                                                                                                                                                                                                                                         |        | Cyclosporin <sup>1</sup> <sub>t</sub>                                                                                                                                        |
| Pentoxifyllin      | 14             |                                                                       | <del>mdr1</del> <sup>1</sup> <sub>vt</sub>                                                                                           | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub> |       |       |       |       |                                                                                  |                                                                                                                                                                                                                                         |        |                                                                                                                                                                              |



|               |    |                           |                                                                                                                                                                |                          |         |  |  |  |  |                                                                                                                               |  |                                                                                    |
|---------------|----|---------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|---------|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------|--|------------------------------------------------------------------------------------|
| Perazin       | 1  |                           |                                                                                                                                                                |                          |         |  |  |  |  | $X_{vt}^1$                                                                                                                    |  |                                                                                    |
| Pergolid      | 1  |                           |                                                                                                                                                                |                          |         |  |  |  |  | $X_{vt}^1$                                                                                                                    |  |                                                                                    |
| Perhexilin    | 1  |                           |                                                                                                                                                                |                          |         |  |  |  |  |                                                                                                                               |  |                                                                                    |
| Perphenazin   | 4  |                           |                                                                                                                                                                | $X_{vt}^1$<br>$X_{vt}^2$ |         |  |  |  |  | $X_{vt}^3$                                                                                                                    |  |                                                                                    |
| Phenacetin    | 2  |                           |                                                                                                                                                                |                          |         |  |  |  |  |                                                                                                                               |  |                                                                                    |
| Phenformin    | 0  |                           |                                                                                                                                                                |                          |         |  |  |  |  |                                                                                                                               |  |                                                                                    |
| Phenobarbital | 35 | $Pgp_{vt}^1$<br>$Pgp_t^2$ | $Pgp_{vt}^1$<br>$Pgp_t^2$<br>$Pgp_{vt}^3$<br>$Pgp, MRP2_{vt}^4$<br>$MDR1, MRP2,$<br>$BCRP,$<br>$MRP6_{vt}^5$<br>$MDR1_{vt}^6$<br>$Pgp, MRP1,$<br>$MRP2_{vt}^7$ |                          |         |  |  |  |  | $X_r^8$<br>$X_r^9$<br>$X_r^{10}$<br>$X_t^{11}$<br>$X_t^{12}$<br>$X_{vt}^{13}$<br>$X_{vt}^{14}$<br>$X_r^{15}$<br>$X_{vt}^{16}$ |  |                                                                                    |
| Phenprocoumon | 5  |                           |                                                                                                                                                                |                          |         |  |  |  |  |                                                                                                                               |  | St John`s<br>wort <sup>1, 2, 3, 4</sup> <sub>r, r, r, r</sub>                      |
| Phenylbutazon | 6  |                           |                                                                                                                                                                |                          |         |  |  |  |  |                                                                                                                               |  |                                                                                    |
| Phenytoin     | 51 | $Pgp_{vt}^1$<br>$Pgp_t^2$ | $Pgp_{vt}^1$<br>$Pgp_t^2$<br>$MDR1, Pgp_{vt}^3$<br>$Pgp, MRP1,$<br>$MRP2_{vt}^4$                                                                               |                          | $X_r^5$ |  |  |  |  | $X_{vt}^6$<br>$X_r^7$<br>$X_{vt}^8$<br>$X_r^9$<br>$X_{vt}^{10}$<br>$X_t^{11}$<br>$X_t^{12}$<br>$X_r^{13}$<br>$X_{vt}^{14}$    |  | Piperine <sup>7</sup> <sub>r</sub><br>St John`s<br>wort <sup>15</sup> <sub>r</sub> |
| Pimecrolimus  | 0  |                           |                                                                                                                                                                |                          |         |  |  |  |  |                                                                                                                               |  |                                                                                    |
| Pilocarpin    | 8  |                           |                                                                                                                                                                |                          |         |  |  |  |  |                                                                                                                               |  |                                                                                    |
| Pimozid       | 5  |                           |                                                                                                                                                                |                          |         |  |  |  |  | $X_{vt}^1$<br>$X_r^2$                                                                                                         |  |                                                                                    |
| Pindolol      | 0  |                           |                                                                                                                                                                |                          |         |  |  |  |  |                                                                                                                               |  |                                                                                    |
| Pioglitazone  | 3  |                           |                                                                                                                                                                |                          |         |  |  |  |  |                                                                                                                               |  |                                                                                    |

|              |     |  |                                |                              |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  |                                                                                                                                                                                                                              |                                                                                                                                                                |  |                                                                                 |
|--------------|-----|--|--------------------------------|------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|--|---------------------------------------------------------------------------------|
| Piroxicam    | 2   |  |                                |                              |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  |                                                                                                                                                                                                                              |                                                                                                                                                                |  |                                                                                 |
| Prajmalin    | 0   |  |                                |                              |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  |                                                                                                                                                                                                                              |                                                                                                                                                                |  |                                                                                 |
| Pramipexol   | 0   |  |                                |                              |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  |                                                                                                                                                                                                                              |                                                                                                                                                                |  |                                                                                 |
| Praziquantel | 2   |  |                                |                              |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  |                                                                                                                                                                                                                              | X <sup>1</sup> <sub>vt</sub>                                                                                                                                   |  |                                                                                 |
| Pravastatin  | 30  |  | Pgp <sup>1</sup> <sub>vt</sub> |                              |                                                                                                                                                                                                                                                                                                                              | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>t</sub>                                     |  |  | X <sup>2</sup> <sub>vt</sub>                                                                                                                                                                                                 | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>t</sub><br>X <sup>4</sup> <sub>vt</sub>                                                                    |  | Colchizin <sup>5</sup> <sub>h</sub><br>St John`s wort <sup>6</sup> <sub>r</sub> |
| Prazepam     | 0   |  |                                |                              |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  |                                                                                                                                                                                                                              |                                                                                                                                                                |  |                                                                                 |
| Prazosin     | 63  |  |                                |                              |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub> | X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>vt</sub> |  | Polyphenole <sup>2</sup> <sub>vt</sub><br>Gomisin A <sup>12</sup> <sub>vt</sub> |
| Prednisolon  | 53  |  | Pgp <sup>1</sup> <sub>t</sub>  |                              |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  |                                                                                                                                                                                                                              | X <sup>2</sup> <sub>vt</sub>                                                                                                                                   |  | Cyclo-<br>sporin A <sup>3</sup> <sub>h</sub>                                    |
| Prednison    | 64  |  | Pgp <sup>1</sup> <sub>h</sub>  |                              |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  |                                                                                                                                                                                                                              | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>h</sub><br>X <sup>5</sup> <sub>vt</sub>                                     |  |                                                                                 |
| Pregabalin   | 0   |  |                                |                              |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  |                                                                                                                                                                                                                              |                                                                                                                                                                |  |                                                                                 |
| Primaquin    | 3   |  |                                | X <sup>1</sup> <sub>vt</sub> |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  |                                                                                                                                                                                                                              |                                                                                                                                                                |  |                                                                                 |
| Primidon     | 1   |  |                                |                              |                                                                                                                                                                                                                                                                                                                              |                                                                                                 |  |  |                                                                                                                                                                                                                              |                                                                                                                                                                |  |                                                                                 |
| Probenicid   | 147 |  |                                |                              | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>h</sub><br>X <sup>10</sup> <sub>vt</sub> | X <sup>13</sup> <sub>vt</sub><br>X <sup>14</sup> <sub>vt</sub><br>X <sup>15</sup> <sub>vt</sub> |  |  |                                                                                                                                                                                                                              |                                                                                                                                                                |  | Morphine-6-<br>glucuronid<br>(M6G) <sup>9</sup> <sub>h</sub>                    |

|             |     |                                                                                                           |                                     |  |                                                                |                              |  |  |                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                   |                                                                                        |
|-------------|-----|-----------------------------------------------------------------------------------------------------------|-------------------------------------|--|----------------------------------------------------------------|------------------------------|--|--|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
|             |     |                                                                                                           |                                     |  | X <sup>11</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>vt</sub> |                              |  |  |                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                   |                                                                                        |
| Procainamid | 4   |                                                                                                           |                                     |  |                                                                |                              |  |  |                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                   |                                                                                        |
| Progesteron | 163 | Pgp-ATPase <sup>1</sup> <sub>vt</sub><br>Pgp <sup>2</sup> <sub>vt</sub><br>Pgp <sup>3</sup> <sub>vt</sub> | MDR1 <sup>3</sup> <sub>vt</sub>     |  |                                                                | X <sup>4</sup> <sub>vt</sub> |  |  |                              | X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>vt</sub><br>X <sup>13</sup> <sub>vt</sub><br>X <sup>14</sup> <sub>r</sub><br>X <sup>15</sup> <sub>vt</sub>                                                                                                                                 | Kein Substrat <sup>14</sup> <sub>r</sub>                                                                                                                          | Schisandrol<br>A <sup>16</sup> <sub>vt</sub><br>Cholesterol <sup>17</sup> <sub>r</sub> |
| Proguanil   | 1   |                                                                                                           |                                     |  |                                                                |                              |  |  |                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                   |                                                                                        |
| Promethazin | 6   |                                                                                                           | mdr/MDR1 <sup>1</sup> <sub>vt</sub> |  |                                                                |                              |  |  |                              | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                      | “hemmende Wirkung” <sup>2</sup>                                                                                                                                   |                                                                                        |
| Propafenon  | 30  |                                                                                                           |                                     |  |                                                                |                              |  |  | X <sup>1</sup> <sub>vt</sub> | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>vt</sub><br>X <sup>13</sup> <sub>vt</sub><br>X <sup>14</sup> <sub>vt</sub><br>X <sup>15</sup> <sub>h</sub> | Modulator <sup>2, 3, 11</sup><br>„Propafenon-Typ“:<br>1, 2, 3, 6, 8, 9, 12, 13, 14<br><br>5-Hydroxypropafenon ist<br>ein Pgp-Substrat <sup>10</sup> <sub>vt</sub> | Grapefruit-<br>Saft <sup>16</sup> <sub>r</sub>                                         |
| Propofol    | 4   |                                                                                                           |                                     |  |                                                                |                              |  |  |                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                   |                                                                                        |

|                              |                |                                         |                                                                                                      |            |       |       |       |       |        |                                                                                                                                                                                                     |                                                                                |                                                      |
|------------------------------|----------------|-----------------------------------------|------------------------------------------------------------------------------------------------------|------------|-------|-------|-------|-------|--------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|------------------------------------------------------|
| Propranolol                  | 53             |                                         | Pgp <sup>1</sup> <sub>vt</sub>                                                                       |            |       |       |       |       |        | X <sup>1</sup> <sub>vt</sub><br><del>X<sup>2</sup><sub>vt</sub></del><br>X <sup>3</sup> <sub>t</sub><br>X <sup>4</sup> <sub>vt</sub><br><del>X<sup>5</sup><sub>vt</sub></del>                       | Kein Pgp-Substrat <sup>6</sup> <sub>vt, 7</sub> <sub>vt, 8</sub> <sub>vt</sub> |                                                      |
| Pyrimethamin                 | 10             |                                         |                                                                                                      |            |       |       |       |       |        |                                                                                                                                                                                                     |                                                                                |                                                      |
| Substanz                     | Anzahl Artikel | Wirkung auf Funktion von                | Wirkung auf Expression von                                                                           | MDR-Umkehr | MRP 1 | MRP 2 | MRP 3 | MRP 4 | BCRP 1 | Pgp                                                                                                                                                                                                 | Zusatz                                                                         | Wechselwirkungen                                     |
| Guanoxan                     | 0              |                                         |                                                                                                      |            |       |       |       |       |        |                                                                                                                                                                                                     |                                                                                |                                                      |
| Quetiapin                    | 7              |                                         |                                                                                                      |            |       |       |       |       |        | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>r</sub><br><del>X<sup>4</sup><sub>vt</sub></del>                                                                | Kein Pgp-Substrat <sup>5</sup> <sub>vt</sub>                                   |                                                      |
| Quinidin<br>-siehe Chinidin- |                |                                         |                                                                                                      |            |       |       |       |       |        |                                                                                                                                                                                                     |                                                                                |                                                      |
| Quinin<br>-siehe Chinin-     |                |                                         |                                                                                                      |            |       |       |       |       |        |                                                                                                                                                                                                     |                                                                                |                                                      |
| Quinupristin                 | 0              |                                         |                                                                                                      |            |       |       |       |       |        |                                                                                                                                                                                                     |                                                                                |                                                      |
|                              |                |                                         |                                                                                                      |            |       |       |       |       |        |                                                                                                                                                                                                     |                                                                                |                                                      |
| Rabeprazol                   | 4              |                                         |                                                                                                      |            |       |       |       |       |        |                                                                                                                                                                                                     |                                                                                |                                                      |
| Ranitidin                    | 12             |                                         |                                                                                                      |            |       |       |       |       |        | X <sup>1</sup> <sub>vt</sub><br><del>X<sup>2</sup><sub>vt</sub></del><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>t</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>h</sub> |                                                                                | Rifampicin,<br>Ketoconazol <sup>6</sup> <sub>h</sub> |
| Rauchen<br>(Tobacco)         | 21             | <del>Pgp<sup>1</sup><sub>vt</sub></del> | MDR1-Gen <sup>2</sup> <sub>h</sub><br>Pgp <sup>3</sup> <sub>t</sub><br>Pgp <sup>4</sup> <sub>t</sub> |            |       |       |       |       |        |                                                                                                                                                                                                     |                                                                                | Indol-3-Carbinol <sup>4</sup> <sub>t</sub>           |
| Reboxetin                    | 1              |                                         |                                                                                                      |            |       |       |       |       |        | <del>X<sup>1</sup><sub>vt</sub></del>                                                                                                                                                               |                                                                                |                                                      |
| Repaglinid                   | 5              |                                         |                                                                                                      |            |       |       |       |       |        | <del>X<sup>1</sup><sub>vt</sub></del>                                                                                                                                                               |                                                                                | Grapefruit-Saft <sup>2</sup> <sub>r</sub>            |
| Retigabin                    | 0              |                                         |                                                                                                      |            |       |       |       |       |        |                                                                                                                                                                                                     |                                                                                |                                                      |
| Rifabutin                    | 7              |                                         |                                                                                                      |            |       |       |       |       |        |                                                                                                                                                                                                     |                                                                                | Antiretrovirale Erreger <sup>1</sup> <sub>r</sub>    |

|                         |     |                                |                                |  |                             |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |                                                                                                                                          |
|-------------------------|-----|--------------------------------|--------------------------------|--|-----------------------------|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|------------------------------------------------------------------------------------------------------------------------------------------|
| Rifampicin/<br>Rifampin | 117 |                                |                                |  |                             |  |  |  |  | X <sup>1</sup> <sub>r</sub><br>X <sup>2</sup> <sub>r</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>r</sub><br>X <sup>5</sup> <sub>r</sub>                                                                                                                                                                                                                                                                                                                                                                        |  | Piperin <sup>6</sup> <sub>r</sub>                                                                                                        |
| Rifapentin              | 0   |                                |                                |  |                             |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |                                                                                                                                          |
| Riluzol                 | 1   |                                |                                |  |                             |  |  |  |  | X <sup>1</sup> <sub>t</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |  |                                                                                                                                          |
| Risperidon              | 27  |                                |                                |  |                             |  |  |  |  | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>t</sub><br>X <sup>3</sup> <sub>t</sub><br>X <sup>4</sup> <sub>t</sub><br>X <sup>5</sup> <sub>t</sub><br>X <sup>6</sup> <sub>t, vt</sub><br>X <sup>7</sup> <sub>t</sub><br>X <sup>8</sup> <sub>r</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>r</sub><br>X <sup>11</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>r</sub><br>X <sup>13</sup> <sub>t, vt</sub><br>X <sup>14</sup> <sub>r</sub><br>X <sup>15</sup> <sub>t</sub><br>X <sup>16</sup> <sub>t</sub> |  | Sertralin <sup>7</sup> <sub>t</sub><br>Rifampin <sup>17</sup> <sub>h</sub>                                                               |
| Ritonavir               | 123 | Pgp <sup>1</sup> <sub>r</sub>  |                                |  | X <sup>1</sup> <sub>r</sub> |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  | St John`s wort <sup>2</sup> <sub>r</sub><br>Pflanzl. Arznei-<br>mittel <sup>3</sup> <sub>r</sub><br>Cloroquin <sup>4</sup> <sub>vt</sub> |
| Rofecoxib               | 2   | Pgp <sup>1</sup> <sub>vt</sub> | Pgp <sup>1</sup> <sub>vt</sub> |  |                             |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |                                                                                                                                          |
| Ropinirol               | 0   |                                |                                |  |                             |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |                                                                                                                                          |
| Ropivacain              | 2   |                                |                                |  |                             |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |                                                                                                                                          |
| Rosiglitazon            | 2   |                                |                                |  |                             |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |                                                                                                                                          |
| Roxithromy-<br>cin      | 7   |                                |                                |  |                             |  |  |  |  | X <sup>1</sup> <sub>h</sub><br>X <sup>2</sup> <sub>h</sub><br>X <sup>3</sup> <sub>h</sub><br>X <sup>4</sup> <sub>h, vt</sub>                                                                                                                                                                                                                                                                                                                                                                                                   |  |                                                                                                                                          |

|                                 |                       |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                           |
|---------------------------------|-----------------------|---------------------------------|---------------------------------------|-------------------|-------------------------------------------------------------------------------------------------|--------------------------------------------------------------|--------------|--------------|--------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| R-Warfarin                      | 1                     |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                           |
|                                 |                       |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                           |
| <b>Substanz</b>                 | <b>Anzahl Artikel</b> | <b>Wirkung auf Funktion von</b> | <b>Wirkung auf Expression von</b>     | <b>MDR-Umkehr</b> | <b>MRP 1</b>                                                                                    | <b>MRP 2</b>                                                 | <b>MRP 3</b> | <b>MRP 4</b> | <b>BCRP 1</b>                                                | <b>Pgp</b>                                                                                                                                                                                                                                                                                                                                                                                            | <b>Zusatz</b>                                                                                                                                                           | <b>Wechselwirkungen</b>                                                                                                                                                                                                                                                                                   |
| Salbutamol<br>-siehe Albuterol- |                       |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                           |
| Salmeterol                      | 1                     |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                           |
| Saquinavir                      | 102                   |                                 | Pgp <sup>1</sup> <sub>vt</sub>        |                   | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>t, vt</sub><br>X <sup>4</sup> <sub>vt</sub> | X <sup>2</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub> |              |              | X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub> | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>t, vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>vt</sub><br>X <sup>13</sup> <sub>vt</sub><br>X <sup>14</sup> <sub>vt</sub><br>X <sup>15</sup> <sub>vt</sub> |                                                                                                                                                                         | Grapefruit-Saft,<br>Orangensaft <sup>2</sup> <sub>vt</sub><br>Mefloquin <sup>16</sup> <sub>vt</sub><br>St John`s wort <sup>17</sup> <sub>r</sub><br>Pflanzl.<br>Arzneimittel <sup>18</sup> <sub>r</sub><br>Lopinavir,<br>Atazanavir <sup>19</sup> <sub>vt</sub><br>Chloroquin <sup>20</sup> <sub>vt</sub> |
| Secobarbital                    | 0                     |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                           |
| Selegilin                       | 2                     |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                           |
| Sertindol                       | 1                     |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                           |
| Sertralin                       | 7                     |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>h</sub><br>X <sup>3</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                           | Von geringer klinischer Bedeutung <sup>2</sup>                                                                                                                          | Risperidon <sup>4</sup> <sub>t</sub><br>St John`s wort <sup>5</sup> <sub>r</sub>                                                                                                                                                                                                                          |
| Sevofluran                      | 0                     |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                           |
| Sibutramin                      | 1                     |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                         | Grapefruit-Saft <sup>1</sup> <sub>rcop</sub>                                                                                                                                                                                                                                                              |
| Sildenafil                      | 3                     |                                 |                                       |                   |                                                                                                 |                                                              |              |              |                                                              |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                         | Grapefruit-Saft <sup>1</sup> <sub>rcop</sub>                                                                                                                                                                                                                                                              |
| Simvastatin                     | 30                    |                                 | mdr2, mdr1b <sup>1</sup> <sub>t</sub> |                   |                                                                                                 | X <sup>6</sup> <sub>vt</sub>                                 |              |              |                                                              | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                           | Substrat von Pgp <sup>7</sup> <sub>r</sub><br>Lacton-Form ist Substrat von Pgp <sup>8</sup><br>Interaktion mit Pgp <sup>9</sup> <sub>vt</sub><br>Kein Einfluss auf Pgp/ | Itraconazol <sup>3</sup> <sub>r</sub><br>cop<br>Rifampin <sup>11</sup> <sub>rcop</sub><br><sup>12</sup> <sub>rcop</sub> , <sup>13</sup> <sub>rcop</sub><br>St John`s                                                                                                                                      |

|                                       |    |  |                                                                                                 |                              |                              |                             |  |  |                              |                                                                                                                                                                                                                                                                                                                                                                                                                           |                                 |                                                                                                                                                                                                                                                                                                                                                                                      |
|---------------------------------------|----|--|-------------------------------------------------------------------------------------------------|------------------------------|------------------------------|-----------------------------|--|--|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                       |    |  |                                                                                                 |                              |                              |                             |  |  |                              | X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>r</sub><br>X <sup>8</sup> <sub>t</sub>                                                                                                                                                                                                                                                                                                                                | Mrp2 <sup>10</sup> <sub>h</sub> | wort <sup>14</sup> <sub>rcop</sub> , <sup>15</sup> <sub>r</sub> ,<br><sup>16</sup> <sub>rcop</sub><br>Grapefruit-<br>Saft <sup>17</sup> <sub>rcop</sub><br>Clarithromy-<br>cin/Erythro-<br>mycin <sup>18</sup> <sub>h</sub>                                                                                                                                                          |
| Sirolimus                             | 52 |  |                                                                                                 | X <sup>10</sup> <sub>h</sub> | X <sup>1</sup> <sub>vt</sub> |                             |  |  | X <sup>1</sup> <sub>vt</sub> | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>h</sub><br>X <sup>7</sup> <sub>r</sub><br>X <sup>8</sup> <sub>h</sub><br>X <sup>9</sup> <sub>h</sub><br>X <sup>10</sup> <sub>h</sub><br>X <sup>11</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>h</sub><br>X <sup>13</sup> <sub>r</sub> |                                 | Itraconazol,<br>Fluconazol,<br>Erythromycin,<br>Voriconazol <sup>7</sup> <sub>r</sub><br>Diltiazem,<br>Erythromycin,<br>Ketoconazol,<br>Verapamil,<br>Cyclosporin,<br>Rifampin <sup>9</sup> <sub>h</sub><br>Amiodaron <sup>12</sup> <sub>h</sub><br>Cyclosporin<br>A <sup>14</sup> <sub>tcop</sub> , <sup>10</sup> <sub>h</sub><br>Clarithro-<br>mycin <sup>15</sup> <sub>hcop</sub> |
| S-Mephenytoin                         | 8  |  |                                                                                                 |                              |                              |                             |  |  |                              |                                                                                                                                                                                                                                                                                                                                                                                                                           |                                 |                                                                                                                                                                                                                                                                                                                                                                                      |
| Sparfloxacin                          | 11 |  |                                                                                                 | X <sup>1</sup> <sub>vt</sub> |                              |                             |  |  |                              | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>t</sub><br>X <sup>5</sup> <sub>t, vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>t, vt</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>r</sub>                                                                                                                                                          |                                 |                                                                                                                                                                                                                                                                                                                                                                                      |
| Sparteine                             | 2  |  |                                                                                                 |                              |                              |                             |  |  |                              |                                                                                                                                                                                                                                                                                                                                                                                                                           |                                 |                                                                                                                                                                                                                                                                                                                                                                                      |
| Spiramycin                            | 1  |  |                                                                                                 |                              |                              | X <sup>1</sup> <sub>t</sub> |  |  |                              | X <sup>1</sup> <sub>t</sub>                                                                                                                                                                                                                                                                                                                                                                                               |                                 |                                                                                                                                                                                                                                                                                                                                                                                      |
| St.-John's<br>wort<br>(Johanniskraut) | 67 |  | Pgp <sup>1</sup> <sub>r</sub><br>Pgp <sup>2</sup> <sub>r</sub><br>Pgp <sup>3</sup> <sub>r</sub> |                              |                              |                             |  |  |                              | X <sup>4</sup> <sub>r</sub><br>X <sup>5</sup> <sub>r</sub><br>X <sup>6</sup> <sub>r</sub>                                                                                                                                                                                                                                                                                                                                 |                                 |                                                                                                                                                                                                                                                                                                                                                                                      |

|                          |                       |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
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|                          |                       |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               | X <sup>7</sup> <sub>r</sub><br>X <sup>8</sup> <sub>r</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>r</sub>                                                             |               |                                                                                                                                                                                                                                     |
| Stavudin                 | 6                     |                                 | MDR1 <sup>1</sup> <sub>vt</sub>   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
| Sufentanil               | 2                     |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                           |               |                                                                                                                                                                                                                                     |
| Sulfadiazin              | 1                     |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
| Sulfafurazol             | 0                     |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
| Sulfamethazin            | 0                     |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
| Sulfameth-oxazol         | 4                     |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
| Sulfaphenazol            | 2                     |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
| Sulfinpyrazon            | 18                    |                                 |                                   |                   | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>vt</sub> | X <sup>2</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>vt</sub> |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
| Suprofen                 | 0                     |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
| S-Warfarin               | 3                     |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
| <b>Substanz</b>          | <b>Anzahl Artikel</b> | <b>Wirkung auf Funktion von</b> | <b>Wirkung auf Expression von</b> | <b>MDR-Umkehr</b> | <b>MRP 1</b>                                                                                                                                                                                                                                                                                 | <b>MRP 2</b>                                                                                   | <b>MRP 3</b> | <b>MRP 4</b> | <b>BCRP 1</b> | <b>Pgp</b>                                                                                                                                                                             | <b>Zusatz</b> | <b>Wechselwirkungen</b>                                                                                                                                                                                                             |
| Tabak<br>-siehe Rauchen- |                       |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
| Tacrin                   | 1                     |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               |                                                                                                                                                                                        |               |                                                                                                                                                                                                                                     |
| Tacrolimus               | 186                   |                                 |                                   |                   |                                                                                                                                                                                                                                                                                              |                                                                                                |              |              |               | X <sup>1</sup> <sub>r</sub><br>X <sup>2</sup> <sub>r</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>r</sub><br>X <sup>5</sup> <sub>r</sub><br>X <sup>6</sup> <sub>r</sub> |               | St John`s wort <sup>1</sup> <sub>r</sub> , <sup>9</sup> <sub>rcop</sub> , <sup>10</sup> <sub>r</sub><br><sup>11</sup> <sub>rcop</sub> , <sup>12</sup> <sub>rcop</sub><br>Pflanzl.<br>Arzneimittel <sup>13</sup> <sub>r</sub><br>cop |



|                             |     |  |                                     |                               |            |            |            |            |            |                                                                                    |                                                                                     |                                                                             |
|-----------------------------|-----|--|-------------------------------------|-------------------------------|------------|------------|------------|------------|------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
|                             |     |  |                                     |                               |            |            |            |            |            | $X_r^7$<br>$X_r^8$                                                                 |                                                                                     |                                                                             |
| Tamoxifen                   | 144 |  | MDR1 <sup>1</sup> <sub>vt</sub>     | $X_t^2$<br>$X_r^3$<br>$X_h^4$ |            |            |            |            |            | $X_{vt}^1$<br>$X_{vt}^5$<br>$X_t^6$<br>$X_h^7$<br>$X_h^8$<br>$X_h^9$<br>$X_t^{10}$ | Modulator von Pgp <sup>11</sup> <sub>vt</sub> ,<br><sup>12</sup> <sub>vt</sub>      | Quercetin <sup>7</sup> <sub>h</sub><br>Kaempferol <sup>9</sup> <sub>h</sub> |
| Tamsulosin                  | 0   |  |                                     |                               |            |            |            |            |            |                                                                                    |                                                                                     |                                                                             |
| Taxol<br>-siehe Paclitaxel- |     |  |                                     |                               |            |            |            |            |            |                                                                                    |                                                                                     |                                                                             |
| Teerstoffe<br>-siehe Tabak- |     |  |                                     |                               |            |            |            |            |            |                                                                                    |                                                                                     |                                                                             |
| Telithromycin               | 6   |  |                                     |                               |            | $X_{vt}^1$ |            |            |            | $X_{vt}^1$<br>$X_{vt}^2$<br>$X_h^3$<br>$X_{h, vt}^4$<br>$X_{vt}^1$                 |                                                                                     |                                                                             |
| Telmisartan                 | 1   |  |                                     |                               |            |            |            |            |            |                                                                                    |                                                                                     |                                                                             |
| Temazepam                   | 0   |  |                                     |                               |            |            |            |            |            |                                                                                    |                                                                                     |                                                                             |
| Teniposid                   | 49  |  | MRP, Pgp <sup>1</sup> <sub>vt</sub> |                               | $X_{vt}^2$ |            |            |            | $X_{vt}^3$ | $X_{vt}^2$<br>$X_r^4$                                                              | Resistenz/Kreuzresistenz<br>in allen Artikeln                                       |                                                                             |
| Tenofovir                   | 7   |  |                                     |                               | $X_{vt}^1$ | $X_{vt}^1$ | $X_{vt}^1$ | $X_{vt}^2$ |            | $X_v^3$<br>$X_{vt}^4$<br>$X_{vt}^5$                                                | Pro-Pharmakon <sup>3, 4</sup>                                                       | Protease- Inhi-<br>bitoren <sup>5</sup> <sub>vt</sub>                       |
| Tenoxicam                   | 0   |  |                                     |                               |            |            |            |            |            |                                                                                    |                                                                                     |                                                                             |
| Terbinafin                  | 3   |  |                                     |                               |            |            |            |            |            |                                                                                    | Zusammenhang mit<br>MRP1, MRP2 bei Leber-<br>intoxikation <sup>1</sup> <sub>r</sub> |                                                                             |
| Terfenadin                  | 60  |  |                                     |                               |            |            |            |            |            | $X_{vt}^1$<br>$X_{vt}^2$<br>$X_{vt}^3$<br>$X_{vt}^4$<br>$X_{vt}^5$                 |                                                                                     | Ketoconazol <sup>7</sup> <sub>vt</sub>                                      |

|             |    |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
|-------------|----|--|-----------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|             |    |  |                                               |                                                                                                                             |  |  |  |  |  | X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub>                               |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Testosteron | 45 |  | Pgp, MRP2 <sup>1</sup> <sub>t</sub>           |                                                                                                                             |  |  |  |  |  | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub>                                                               | Modulator von Pgp <sup>4</sup> <sub>vt</sub>                                                                                                                                                              | Rifampin <sup>5</sup> <sub>vt</sub>                                                                                                                                                                                             |
| Tetracyclin | 15 |  | MDR1<br>cDNA <sup>1</sup> <sub>vt</sub>       |                                                                                                                             |  |  |  |  |  | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub>                                                               |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Theophyllin | 23 |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           | St John`s wort-<br>cop <sup>1</sup> <sub>r</sub> , <sup>2</sup> <sub>r</sub> , <sup>3</sup> <sub>r</sub> , <sup>4</sup> <sub>r</sub><br>Antiinfektiva <sup>5</sup> <sub>r</sub><br>cop<br>Rifampin <sup>6</sup> <sub>rcop</sub> |
| Thiamazol   | 0  |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Thioridazin | 5  |  |                                               | X <sup>1</sup> <sub>vt</sub>                                                                                                |  |  |  |  |  | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub>                                                               |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Thiotepa    | 6  |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Thiothixen  | 0  |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Tiabendazol | 4  |  |                                               |                                                                                                                             |  |  |  |  |  | X <sup>1</sup> <sub>vt</sub>                                                                                               |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Tiagabin    | 1  |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Ticlopidin  | 2  |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Timolol     | 2  |  |                                               |                                                                                                                             |  |  |  |  |  | X <sup>1</sup> <sub>vt</sub>                                                                                               |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Tizanidin   | 0  |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Tocainid    | 0  |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Tolbutamid  | 12 |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           | St John`s<br>wort <sup>1</sup> <sub>rcop</sub>                                                                                                                                                                                  |
| Tolcapon    | 0  |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Tolterodin  | 0  |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Topiramat   | 9  |  | mdr1a/mdr1b<br>mRNA <sup>1</sup> <sub>t</sub> |                                                                                                                             |  |  |  |  |  | X <sup>2</sup> <sub>t</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>r</sub>                                  | Kein Substrat von Pgp <sup>5</sup> <sub>vt</sub>                                                                                                                                                          |                                                                                                                                                                                                                                 |
| Torasemid   | 1  |  |                                               |                                                                                                                             |  |  |  |  |  |                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                                                                                                                                 |
| Toremifen   | 17 |  |                                               | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>h</sub> |  |  |  |  |  | X <sup>2</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>h</sub><br>X <sup>9</sup> <sub>h</sub> | Modulator von Pgp <sup>10</sup> <sub>vt</sub> ,<br><sup>11</sup> <sub>t</sub> , <sup>12</sup> <sub>r</sub><br>Chemo-Sensibilisator <sup>13</sup> <sub>vt</sub><br>BCRP-Umkehr <sup>14</sup> <sub>vt</sub> | Tetrandine <sup>5</sup> <sub>vt</sub>                                                                                                                                                                                           |

|                                      |    |                                                                                    |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                              |                              |  |  |  |                              |                                                                                                                                                                                                                                                                                                    |                                                                                                                                          |  |
|--------------------------------------|----|------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|--|--|--|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|--|
|                                      |    |                                                                                    |                                                                                                                                                                                                                                                                                            | X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>r</sub>                                                                                                                                                                                                                                  |                              |  |  |  |                              |                                                                                                                                                                                                                                                                                                    |                                                                                                                                          |  |
| Tramadol                             | 2  |                                                                                    |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                              |                              |  |  |  |                              |                                                                                                                                                                                                                                                                                                    |                                                                                                                                          |  |
| Tranyl-<br>cypromin                  | 0  |                                                                                    |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                              |                              |  |  |  |                              |                                                                                                                                                                                                                                                                                                    |                                                                                                                                          |  |
| Trazodon                             | 1  |                                                                                    | Pgp <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                              |                              |  |  |  |                              |                                                                                                                                                                                                                                                                                                    |                                                                                                                                          |  |
| Tretinoin<br>(= Vitamin A-<br>Säure) | 40 | Pgp <sup>1</sup> <sub>vt</sub><br>Pgp <sup>2</sup> <sub>vt</sub>                   | Pgp <sup>1</sup> <sub>vt</sub><br>Pgp <sup>2</sup> <sub>vt</sub><br>mdr1 mRNA <sup>3</sup> <sub>vt</sub><br>MDR1 <sup>4</sup> <sub>vt</sub><br>MDR1, MRP <sup>5</sup> <sub>vt</sub><br>MDR1 <sup>6</sup> <sub>vt</sub><br>Pgp <sup>7</sup> <sub>vt</sub><br>Pgp <sup>8</sup> <sub>vt</sub> |                                                                                                                                                                                                                                                                                              | X <sup>9</sup> <sub>vt</sub> |  |  |  |                              | X <sup>6</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>r</sub>                                                                                                                                                                      | Zusammen mit Verapa-<br>mil <sup>2</sup><br>Pgp ohne Einfluss auf<br>Retinoide <sup>12</sup> <sub>t, vt</sub>                            |  |
| Triamcinolon                         | 7  |                                                                                    |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                              |                              |  |  |  | X <sup>1</sup> <sub>vt</sub> | X <sup>2</sup> <sub>t</sub>                                                                                                                                                                                                                                                                        |                                                                                                                                          |  |
| Triazolam                            | 14 |                                                                                    |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                              |                              |  |  |  |                              |                                                                                                                                                                                                                                                                                                    |                                                                                                                                          |  |
| Trifluoperazin                       | 59 | Pgp <sup>1</sup> <sub>vt</sub><br>ATPase Aktivi-<br>tät <sup>2</sup> <sub>vt</sub> |                                                                                                                                                                                                                                                                                            | X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>r</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub><br>X <sup>8</sup> <sub>vt</sub><br>X <sup>9</sup> <sub>vt</sub><br>X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>r</sub> |                              |  |  |  |                              | X <sup>12</sup> <sub>vt</sub><br>X <sup>13</sup> <sub>vt</sub><br>X <sup>14</sup> <sub>vt</sub><br>X <sup>15</sup> <sub>vt</sub><br>X <sup>16</sup> <sub>h</sub><br>X <sup>17</sup> <sub>h</sub><br>X <sup>18</sup> <sub>vt</sub><br>X <sup>19</sup> <sub>vt</sub><br>X <sup>20</sup> <sub>r</sub> | Umgehung der Resi-<br>stenz <sup>21</sup> <sub>r</sub><br>Modulator von Pgp <sup>22</sup> <sub>vt</sub> ,<br><sup>23</sup> <sub>vt</sub> |  |
| Trimethoprim                         | 7  |                                                                                    |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                              |                              |  |  |  |                              | X <sup>1</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                       |                                                                                                                                          |  |
| Trimipramin                          | 2  |                                                                                    |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                              |                              |  |  |  |                              | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>t</sub>                                                                                                                                                                                                                                        | Modulator von Pgp <sup>1</sup> <sub>vt</sub>                                                                                             |  |
| Troglitazon                          | 2  |                                                                                    |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                              |                              |  |  |  |                              |                                                                                                                                                                                                                                                                                                    |                                                                                                                                          |  |
| Troleando-<br>mycin                  | 11 |                                                                                    |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                              |                              |  |  |  |                              |                                                                                                                                                                                                                                                                                                    |                                                                                                                                          |  |
| Tropisetron                          | 1  |                                                                                    |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                              |                              |  |  |  |                              |                                                                                                                                                                                                                                                                                                    |                                                                                                                                          |  |

| Urapidil      | 0              |                                                                     |                                                                                                                                           |                                                                                                                          |                              |       |       |       |        |                                                                                                                                                                                         |                                                                 |                                                                                                                                 |
|---------------|----------------|---------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|------------------------------|-------|-------|-------|--------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|
| Substanz      | Anzahl Artikel | Wirkung auf Funktion von                                            | Wirkung auf Expression von                                                                                                                | MDR-Umkehr                                                                                                               | MRP 1                        | MRP 2 | MRP 3 | MRP 4 | BCRP 1 | Pgp                                                                                                                                                                                     | Zusatz                                                          | Wechselwirkungen                                                                                                                |
| Valdecoxib    | 0              |                                                                     |                                                                                                                                           |                                                                                                                          |                              |       |       |       |        |                                                                                                                                                                                         |                                                                 |                                                                                                                                 |
| Valproinsäure | 22             | Pgp <sup>1</sup> <sub>t, vt</sub><br>Pgp <sup>2</sup> <sub>vt</sub> | Pgp <sup>1</sup> <sub>t, vt</sub><br>Pgp <sup>2</sup> <sub>vt</sub><br>MDR1 <sup>3</sup> <sub>vt</sub><br>MDR1 <sup>4</sup> <sub>vt</sub> | X <sup>5</sup> <sub>vt</sub>                                                                                             | X <sup>6</sup> <sub>vt</sub> |       |       |       |        | X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>vt</sub>                                                                                                                            | Kein Substrat von Pgp, MRP1, MRP2 <sup>8</sup> <sub>vt, t</sub> |                                                                                                                                 |
| Valsartan     | 1              |                                                                     |                                                                                                                                           |                                                                                                                          |                              |       |       |       |        |                                                                                                                                                                                         |                                                                 |                                                                                                                                 |
| Vardenafil    | 1              |                                                                     |                                                                                                                                           |                                                                                                                          |                              |       |       |       |        |                                                                                                                                                                                         |                                                                 | Grapefruit-Saft <sup>1</sup> <sub>rcop</sub>                                                                                    |
| Venlafaxin    | 7              |                                                                     | MDR, MRP <sup>1</sup> <sub>vt</sub>                                                                                                       |                                                                                                                          |                              |       |       |       |        | X <sup>2</sup> <sub>vt</sub><br>X <sup>3</sup> <sub>t</sub><br>X <sup>4</sup> <sub>r</sub><br>X <sup>5</sup> <sub>h</sub>                                                               | Schwacher Inhibitor <sup>2</sup>                                | Propafenon <sup>5</sup> <sub>h</sub><br>cop                                                                                     |
| Verapamil     | 2134           |                                                                     |                                                                                                                                           | X <sup>1</sup> <sub>r</sub><br>X <sup>2</sup> <sub>r</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>r</sub> |                              |       |       |       |        | X <sup>5</sup> <sub>r</sub><br>X <sup>6</sup> <sub>r</sub><br>X <sup>7</sup> <sub>r</sub><br>X <sup>8</sup> <sub>r</sub><br>X <sup>9</sup> <sub>r</sub><br>X <sup>10</sup> <sub>r</sub> | Modulator von Pgp <sup>11</sup> <sub>r</sub>                    | Grapefruit-Saft <sup>12</sup> <sub>rcop</sub><br>Rifampin <sup>13</sup> <sub>rcop</sub><br>Sirolimus <sup>14</sup> <sub>h</sub> |
| Vinblastin    | 1073           |                                                                     |                                                                                                                                           |                                                                                                                          |                              |       |       |       |        | X <sup>1</sup> <sub>r</sub><br>X <sup>2</sup> <sub>r</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>r</sub><br>X <sup>6</sup> <sub>r</sub> | cMOAT-Substrat <sup>7</sup> <sub>r</sub>                        | 2-Chlorpromazin <sup>8</sup> <sub>vt</sub><br>Clarithromycin <sup>9</sup> <sub>vt</sub><br>Conferon <sup>10</sup> <sub>vt</sub> |
| Vincristin    | 1019           |                                                                     | Pgp <sup>1</sup> <sub>r</sub>                                                                                                             |                                                                                                                          |                              |       |       |       |        | X <sup>2</sup> <sub>r</sub><br>X <sup>3</sup> <sub>r</sub><br>X <sup>4</sup> <sub>r</sub><br>X <sup>5</sup> <sub>r</sub><br>X <sup>6</sup> <sub>r</sub><br>X <sup>7</sup> <sub>vt</sub> | LRP-Substrat <sup>9</sup> <sub>vt</sub>                         | Itraconazol,<br>Ketoconazol,<br>Cyclosporin,<br>Isoniazid,<br>Nifedipin <sup>10</sup> <sub>rcop</sub>                           |

|                                          |                           |                                         |                                                                 |                              |                              |                  |                  |                  |                   |                                                                                                                                                                                                                            |                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                           |
|------------------------------------------|---------------------------|-----------------------------------------|-----------------------------------------------------------------|------------------------------|------------------------------|------------------|------------------|------------------|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                          |                           |                                         |                                                                 |                              |                              |                  |                  |                  |                   | X <sup>8</sup> <sub>r</sub>                                                                                                                                                                                                |                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                           |
| Vindesin                                 | 39                        |                                         | Pgp <sup>1</sup> <sub>vt</sub><br>Pgp <sup>2</sup> <sub>r</sub> |                              | X <sup>3</sup> <sub>h</sub>  |                  |                  |                  |                   | X <sup>4</sup> <sub>r</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>h</sub>                                                                                                                                 |                                                                                                                     | TNF-alpha <sup>7</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                                                                                      |
| Vinorelbin                               | 32                        |                                         |                                                                 |                              | X <sup>1</sup> <sub>vt</sub> |                  |                  |                  |                   | X <sup>1</sup> <sub>vt</sub><br>X <sup>2</sup> <sub>r</sub><br>X <sup>3</sup> <sub>vt</sub><br>X <sup>4</sup> <sub>vt</sub><br>X <sup>5</sup> <sub>vt</sub><br>X <sup>6</sup> <sub>vt</sub><br>X <sup>7</sup> <sub>r</sub> | Schwaches Substrat <sup>8</sup> <sub>t</sub>                                                                        | Zosuquidar <sup>9</sup> <sub>h</sub>                                                                                                                                                                                                                                                                                                                                      |
| NVB                                      |                           |                                         |                                                                 |                              |                              |                  |                  |                  |                   | X <sup>10</sup> <sub>vt</sub><br>X <sup>11</sup> <sub>vt</sub>                                                                                                                                                             | Navelbin<br>(Vinorelbin Tartrat)                                                                                    |                                                                                                                                                                                                                                                                                                                                                                           |
| Vinflunine                               |                           |                                         |                                                                 |                              |                              |                  |                  |                  |                   | X <sup>4</sup> <sub>vt</sub><br>X <sup>12</sup> <sub>r</sub>                                                                                                                                                               | 20',20'-Difluoro-3',4'-<br>Dihydrovinorelbin<br>Schwächeres Sub-<br>strat/Induktor als Vinorel-<br>bin <sup>4</sup> | Cisplatin, Mi-<br>tomycin C,<br>Doxorubicin,<br>5-Fluoro-<br>uracil <sup>4</sup> <sub>vt</sub>                                                                                                                                                                                                                                                                            |
| Vitamin A-<br>Säure<br>-siehe Tretinoin- |                           |                                         |                                                                 |                              |                              |                  |                  |                  |                   |                                                                                                                                                                                                                            |                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                           |
| Voriconazol                              | 8                         |                                         |                                                                 |                              |                              |                  |                  |                  |                   |                                                                                                                                                                                                                            |                                                                                                                     | St John`s<br>wort <sup>1</sup> <sub>rcop</sub>                                                                                                                                                                                                                                                                                                                            |
| <b>Substanz</b>                          | <b>Anzahl<br/>Artikel</b> | <b>Wirkung auf<br/>Funktion<br/>von</b> | <b>Wirkung auf<br/>Expression<br/>von</b>                       | <b>MDR-<br/>Umkehr</b>       | <b>MRP<br/>1</b>             | <b>MRP<br/>2</b> | <b>MRP<br/>3</b> | <b>MRP<br/>4</b> | <b>BCRP<br/>1</b> | <b>Pgp</b>                                                                                                                                                                                                                 | <b>Zusatz</b>                                                                                                       | <b>Wechsel-<br/>wirkungen</b>                                                                                                                                                                                                                                                                                                                                             |
| Warfarin                                 | 25                        |                                         |                                                                 |                              |                              |                  |                  |                  |                   | X <sup>1</sup> <sub>h</sub>                                                                                                                                                                                                | Möglicherweise <sup>1</sup>                                                                                         | St John`s wort<br>cop <sup>2</sup> <sub>r</sub> , <sup>3</sup> <sub>r</sub> , <sup>4</sup> <sub>r</sub> , <sup>5</sup> <sub>r</sub> ,<br><sup>6</sup> <sub>r</sub><br>Sojamilch <sup>7</sup> <sub>h</sub><br>Pflanzl.<br>Arzneimittel<br>cop <sup>8</sup> <sub>r</sub> , <sup>9</sup> <sub>r</sub> , <sup>10</sup> <sub>r</sub><br>Rifampin <sup>11</sup> <sub>rcop</sub> |
|                                          |                           |                                         |                                                                 |                              |                              |                  |                  |                  |                   |                                                                                                                                                                                                                            |                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                           |
| Yohimbin                                 | 25                        |                                         |                                                                 | X <sup>1</sup> <sub>vt</sub> |                              |                  |                  |                  |                   |                                                                                                                                                                                                                            | Modulator von Pgp <sup>2</sup> <sub>vt</sub>                                                                        |                                                                                                                                                                                                                                                                                                                                                                           |
| Trimethoxyben-                           |                           |                                         | mdr1, Pgp <sup>3</sup> <sub>vt</sub>                            | X <sup>3</sup> <sub>vt</sub> |                              |                  |                  |                  |                   | X <sup>4</sup> <sub>vt</sub>                                                                                                                                                                                               |                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                           |

|                                        |                       |                                 |                                   |                   |              |              |              |              |               |                          |                |                                                                                             |
|----------------------------------------|-----------------------|---------------------------------|-----------------------------------|-------------------|--------------|--------------|--------------|--------------|---------------|--------------------------|----------------|---------------------------------------------------------------------------------------------|
| zoylyohimbin                           |                       |                                 |                                   |                   |              |              |              |              |               |                          |                |                                                                                             |
| Zolmitriptan                           | 5                     |                                 |                                   |                   |              |              |              |              |               | $X^1_{vt}$<br>$X^2_{vt}$ |                | Cetirizin, Flunarizin, Propranolol, Atenolol, Cimetidin, Aspirin <sup>3</sup> <sub>vt</sub> |
| Zolpidem                               | 2                     |                                 |                                   |                   |              |              |              |              |               |                          |                |                                                                                             |
| Zonisamid                              | 2                     |                                 |                                   |                   |              |              |              |              |               |                          |                |                                                                                             |
| Zopiclon                               | 1                     |                                 |                                   |                   |              |              |              |              |               |                          |                |                                                                                             |
| Zotepin                                | 0                     |                                 |                                   |                   |              |              |              |              |               |                          |                |                                                                                             |
| Zuclopenthixol                         | 1                     |                                 |                                   | $X^1_{vt}$        |              |              |              |              |               |                          | „Clopenthixol“ |                                                                                             |
| <b>Substanz</b>                        | <b>Anzahl Artikel</b> | <b>Wirkung auf Funktion von</b> | <b>Wirkung auf Expression von</b> | <b>MDR-Umkehr</b> | <b>MRP 1</b> | <b>MRP 2</b> | <b>MRP 3</b> | <b>MRP 4</b> | <b>BCRP 1</b> | <b>Pgp</b>               | <b>Zusatz</b>  | <b>Wechselwirkungen</b>                                                                     |
| Lipophiles industrielles Lösungsmittel |                       |                                 | $Pgp^1_h$                         |                   |              |              |              |              |               |                          |                |                                                                                             |
| Gemcitabin                             |                       |                                 |                                   |                   |              |              |              |              |               |                          |                | Cortisol <sup>1</sup> <sub>vt</sub>                                                         |

## 4.2 Zusammenfassung der Ergebnisse

Es wurden in der Interaktionstabelle 504 pharmakologische Substanzen auf einen in der Wissenschaft beschriebenen Zusammenhang mit P-Glykoprotein geprüft.

Nach der Auswertung ergaben sich folgende Ergebnisse:

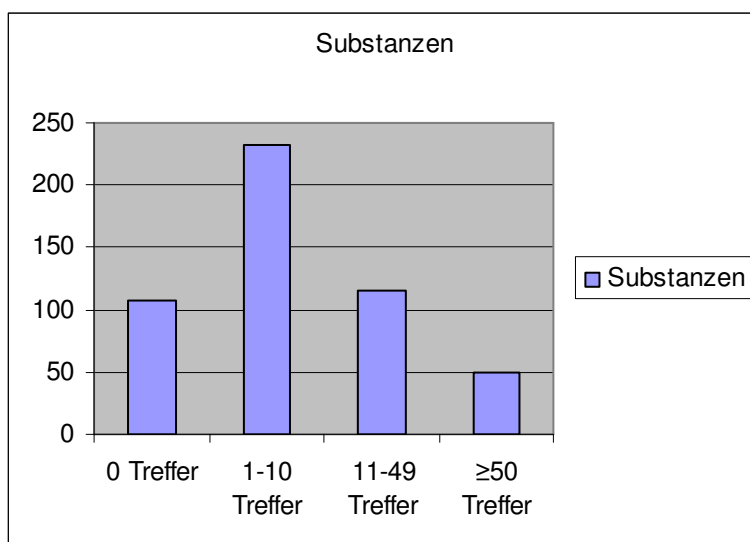
108 Substanzen lieferten keine Treffer bei der Literaturrecherche.

232 Substanzen hatten 1 bis 10 Treffer,

115 Substanzen ergaben 11 bis 49 Treffer und

49 Substanzen lieferten 50 oder mehr Treffer bei der Suche in der Literatur-Datenbank.

Demzufolge hatte die quantitativ größte Gruppe der Arzneimittel bis zu 10 Treffer.



Die Datierung der Artikel ergab folgende Verteilung:

| Zeit          | <1980 | 1981-1990 | 1991-2000 | 2001-2005 | 2006-2008 |
|---------------|-------|-----------|-----------|-----------|-----------|
| Artikelanzahl | -     | 20        | 299       | 617       | 489       |

Der Studienaufbau der Pharmakologen, Biologen und Chemiker, die sich wissenschaftlich mit P-Glykoprotein beschäftigen, war bei 187 Substanzen „vt“, also eine In-vitro-Studie.

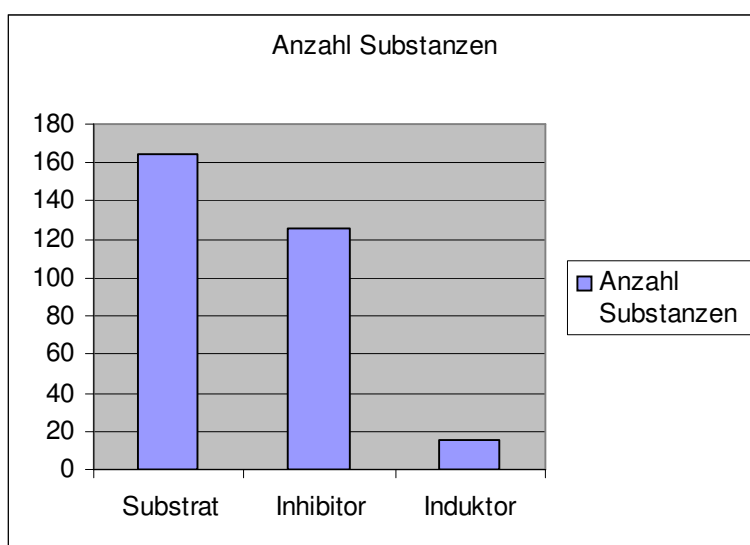
Bei 100 Substanzen fand der Versuch an lebenden Tieren oder mit menschlichen Probanden statt.

| Studienaufbau | vt  | h/t |
|---------------|-----|-----|
| Substanzen    | 187 | 100 |

Bei einer Auszählung der einzelnen Studien in Bezug auf den Studienaufbau zeigte sich, dass die meisten Studien (853), „in vitro“ gestaltet sind, gefolgt von den Artikeln, die eine Zusammenfassung („review“) der aktuellen Studienlage darstellen (247 Studien), darauf folgen die Tierversuche („t“) mit 197 Studien und die Studien mit menschlichen Probanden („h“, 162).

Von 504 sind 164 Substanzen Substrate von P-gp, das bedeutet, sie werden durch das P-Glykoprotein aus Zellen transportiert. 126 Substanzen sind Inhibitoren von P-gp, d.h. sie haben eine hemmende Wirkung auf den Transport von P-gp.

16 Substanzen sind Induktoren von P-gp, das heißt sie haben einen fördernden Effekt auf den Transport von P-gp.





Die Interaktionstabelle ist weiterhin aufgeteilt in Substanzen, die einen fördernden oder hemmenden Effekt auf die **Funktion** von P-gp oder verwandten Transportenzymen haben:

| <b>Fördernder Effekt/Funktion</b> | P-gp | MRP2 | MDR1 | ATPase | BCRP |
|-----------------------------------|------|------|------|--------|------|
| <b>Anzahl Substanzen</b>          | 19   | 3    | 1    | 8      | 1    |

| <b>Hemmender Effekt/Funktion</b> | P-gp | MRP1 | MDR1 | ATPase | P-gp-Aktivität |
|----------------------------------|------|------|------|--------|----------------|
| <b>Anzahl Substanzen</b>         | 13   | 1    | 2    | 2      | 1              |

Die Studien lassen sich in Substanzen mit einem fördernden oder hemmenden Effekt auf die **Expression** von P-gp oder verwandten Transportproteinen aufteilen:

| <b>Fördernder Effekt/Expression</b> | P-gp | MRP1 | MRP2 | MRP4 | MRP5 | MDR1 | MDR2 |
|-------------------------------------|------|------|------|------|------|------|------|
| <b>Anzahl Substanzen</b>            | 41   | 8    | 8    | 2    | 2    | 21   | 4    |

| <b>Fördernder Effekt/Expression</b> | MDR3 | BCRP | mdr1a | mdr1b | P-gp2-mRNA |
|-------------------------------------|------|------|-------|-------|------------|
| <b>Anzahl Substanzen</b>            | 1    | 3    | 1     | 2     | 1          |

| <b>Hemmender Effekt/Expression</b> | P-gp | MRP1 | MRP2 | MRP6 | MDR1 | MDR3 | ABCB1 |
|------------------------------------|------|------|------|------|------|------|-------|
| <b>Anzahl Substanzen</b>           | 14   | 6    | 1    | 1    | 7    | 1    | 1     |

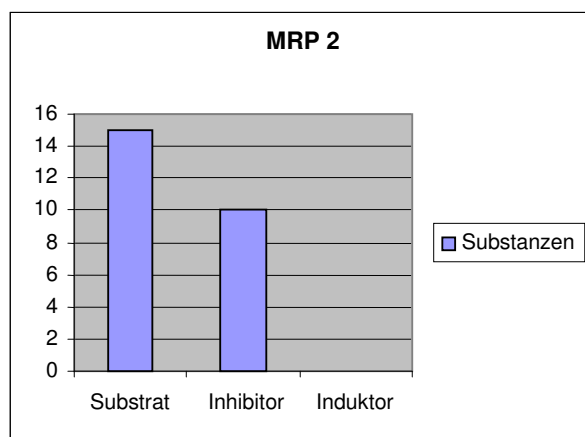
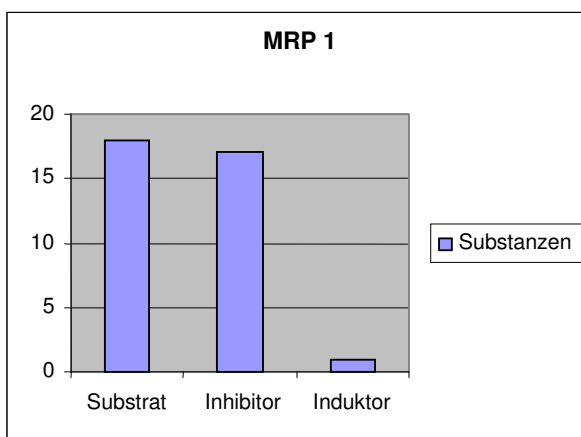
Bei 40 Substanzen ergibt sich nach Sichtung der Literatur eine Wirkung bei der Umkehr der Vielfach-Resistenz (Multi Drug Resistance Reversal).

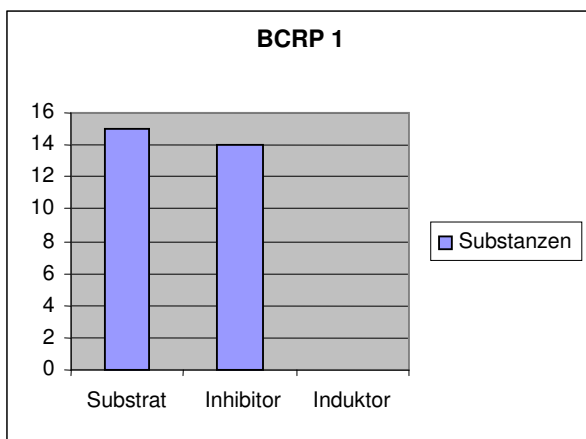
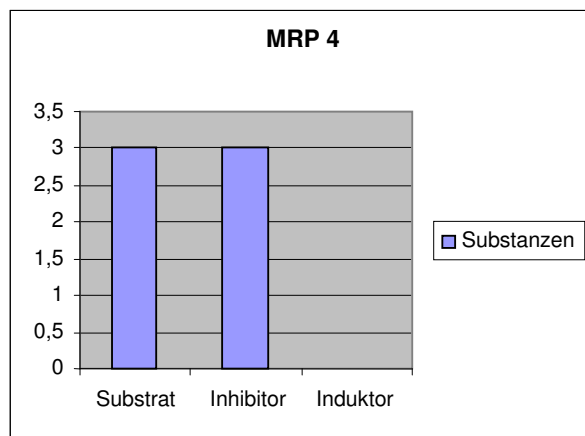
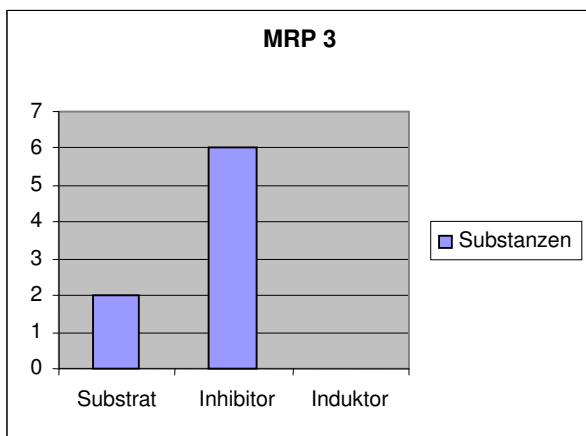
111 Substanzen weisen Wechselwirkungen mit insgesamt 283 anderen Arzneimitteln auf – bei 240 dieser WW ist das P-Glykoprotein an der Entstehung beteiligt, bei den übrigen 43 WW ging aus den bearbeiteten Artikeln nicht hervor, ob die Wechselwirkung über P-gp oder ein CYP-Enzym zustande kommt.

14 Substanzen wurden in Experimenten als Modulatoren von P-gp beschrieben, meist handelte es sich bei diesen Experimenten um pharmakologische und molekulare Studien mit Tumorzellen (Leber, Lunge, Prostata, Brust, Darm) und um eine Beteiligung von P-gp bei der antineoplastischen Chemotherapie.

|                         |                |
|-------------------------|----------------|
| <b>MDR-Umkehr</b>       | 40 Substanzen  |
| <b>Modulatoren</b>      | 14 Substanzen  |
| <b>Wechselwirkungen</b> | 111 Substanzen |

Bei den einzelnen Multidrug-Resistance-related-Proteinen (MRPs) wurde in der Interaktionstabelle wiederum eine Aufteilung der Substanzen in Substrat, Inhibitor und Induktor vorgenommen:





## 5 Diskussion

Die meisten Substanzen haben eine geringe Anzahl von 1-10 Studien im Zusammenhang mit P-Glykoprotein. Hier ist ein weiterer Bedarf an Untersuchungen erkennbar. Bei 28 Substanzen liegt eine vergleichsweise hohe Studienzahl mit  $\geq 100$  vor. Vor allem in den letzten drei Jahren nahm die Zahl der publizierten Arbeiten deutlich zu. Die weitaus meisten Studien sind dabei In-vitro-Studien, die aber unter Umständen nicht über eine gleich hohe Aussagekraft bzgl. der Gefahren einer Wechselwirkung zwischen Medikamenten verfügen wie klinische Studien oder Studien am Menschen. Die Untersuchungen zu P-gp und verwandten Transportenzymen zeigen hinsichtlich der reinen Substrate, Inhibitoren und Induktoren eine ähnliche Verteilung wie man sie auch von den CYP-Enzymen kennt. Dabei überwiegt deutlich die Zahl der Substrate, gefolgt von den Inhibitoren und einer nur geringen Anzahl induzierend wirkender Substanzen. Nur für P-gp und MRP1 wurden Induktoren gefunden. Die Einschätzung des Interaktionspotentials ist aufgrund der vielen In-vitro-Studien schwierig, woraus der Bedarf für weitere Untersuchungen, auch von Interaktionsstudien, gegeben wäre. Dies ist aber unter kontrollierten Bedingungen schwierig in die Praxis umzusetzen.

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## **7 Anhang**

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## 7.2 Curriculum Vitae

### Persönliche Angaben

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|---------------------|-------------------------------------------------------------------|