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# ENVIRONMENTALLY CLASSIFIED PHARMACEUTICALS



**Stockholms läns landsting**

Stockholm County Council

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## Reducing Residues from Pharmaceuticals in Nature is Part of the Environmental Work of Stockholm County Council

Contributing to the reduction of environmental risks from pharmaceuticals is an important part of the environmental work of Stockholm County Council. According to the Environmental Challenge 2016, the Council's 2012-2016 Environmental Programme, the Council is mandated to i.a. do preventive environmental health work. This involves fostering healthy inhabitants in an environment with clean air and water. To reduce the most environmentally hazardous remains of medicinal products in the natural surroundings is therefore an important part of the environmental work of the County Council. One aspect of this work is the assessment and classification of pharmaceuticals according to their impact on the environment.

The pharmaceuticals are classified both in terms of their inherent capacity to affect the environment (environmental hazard), and as regarding the environmental risk posed by the pharmaceutical substances when used to their current extent. The environmental hazard assessment was initiated in 2003 by Environmental Department of the Stockholm County Council. During 2005, the classification was extended to also cover an environmental risk assessment carried out by The Swedish Association of the Pharmaceutical Industry (Lif).

The classification system is used in considering the environmental impact of the pharmaceuticals on the so called Wise List (Kloka Listan), a list of recommended pharmaceuticals for common diseases in Stockholm County Council, issued by the Drug and Therapeutics Committee.

The classification is also available at the website [www.janusinfo.se/environment](http://www.janusinfo.se/environment)

# Impact of Pharmaceuticals on the Environment

The majority of all pharmaceuticals that patients take are excreted in the urine, in unchanged condition or as metabolites, and reach wastewater plants and sometimes even waterways and ground water. Medicines are often adapted to resist biodegradation and can therefore remain in the environment for a long time. Some pharmaceuticals have been found in low, but traceable contents in drinking water, which is a warning sign that the current handling of pharmaceuticals may lead to health and environmental problems in the future.

Access to healthy water is a prerequisite for good health. Since society's use of chemicals, including pharmaceuticals, is continuously growing, the risk is also increasing that these chemicals will return to us in our food and water supply through nature's ecocycle. We have little knowledge of the long-term effects that continuously supplied trace quantities of pharmaceuticals and other chemicals could have on our development, our ability to resist disease and our wellness in general. Therefore caution is advisable. In other words, even if we currently do not have scientific proof that pharmaceuticals in nature can cause health problems, it could be wise to reduce our unintentional exposure to them as much as possible i.e. adhere to the Precautionary Principle, see p.6.

## How the Substances are Classified

Pharmaceutical substances are assessed with respect to environmental hazard and environmental risk. When assessing a medication's environmental impact, consideration should be given to both environmental hazard and environmental risk, as the terms express different properties of the substance.

**Environmental hazard** expresses the inherent environmentally damaging characteristics of the substance in the following terms:

**PERSISTENCE** – ability to resist degradation in the aquatic environment.

**BIOACCUMULATION** – accumulation in adipose tissue of aquatic organisms.

**TOXICITY** – the potential to poison aquatic organisms.

Each of these characteristics is assigned a numerical value (0–3). The total of these values constitutes the PBT Index for the substance. The PBT Index can assume values in the interval 0–9. The hazard model was formulated by Stockholm County Council and Apoteket AB (The National Corporation of Swedish Pharmacies). Since 2006, all information about persistence, bioaccumulation and toxicity is obtained from [www.fass.se](http://www.fass.se).

More information is available at the non-commercial website Janusinfo, produced by the Stockholm County Council:  
[www.janusinfo.se/environment](http://www.janusinfo.se/environment)

**Environmental risk** refers to the risk of toxicity to the aquatic environment. Environmental risk is based on the ratio between predicted environmental concentration of the substance in Swedish water systems (PEC) and the highest concentration of the substance that does not have a harmful effect on the environment (PNEC). Information about the risk is obtained from [www.fass.se](http://www.fass.se).

Risk is specified as:

<b>INSIGNIFICANT</b>	if $PEC/PNEC \leq 0,1$
<b>LOW</b>	if $PEC/PNEC > 0,1 - \leq 1$
<b>MODERATE</b>	if $PEC/PNEC > 1 - \leq 10$
<b>HIGH</b>	if $PEC/PNEC > 10$

## How to Read the Table

**THE SUBSTANCE** can be found under several different drug groups. For example, triamcinolon can be found under "A Alimentary Tract and Metabolism" as well as "D Dermatologicals". Substances indicated in bold are included in "Kloka Listan 2014", Stockholm County Council's "Wise List" of recommended drugs for common diseases (including recommendations for specialized care).

**THE PBT INDEX** is a measure of environmental hazard and can assume all values from 0–9 (the total of P-, B- and the T-value). The higher the value of a substance, the greater its danger to the environment.

**\*(ASTERISK) AFTER THE PBT INDEX** indicates that the assessment is uncertain due to lack of data.

Two substances may have the same risk values but different PBT values, but the risk assessment can also be different even if the PBT values are the same.

When assessing a medication's environmental impact, consideration should be given to both environmental risk and environmental hazard since bioaccumulation and persistence are not included in the risk assessment.

**RISK** refers to toxic risk to the aquatic environment, the calculation based on Swedish conditions and is given as insignificant, low, moderate or high.

"Cannot be excl" means that the manufacturer has stated that the documentary basis for assessment of risk is insufficient. Information about environmental risks can be obtained from [www.fass.se](http://www.fass.se). For risk "exempt", see p.6

**P** (Persistence) can assume the value 0 or 3

**B** (Bioaccumulation) can assume the value 0 or 3

**T** (Toxicity) can assume the value 0–3

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>J Anti-infectives</b> Antibacterials for systemic use <b>trimetoprim</b>	insignificant	4	3	0	1	
<b>erythromycin</b>	insignificant	6	3	0	3	149 661
<b>ofloxacin</b>	insignificant	9*	3	3*	3	C 261 420
<b>amoxicillin</b>	moderate	6	3	0	3	133 025
						1 580
						953 571
						C 272 984

Indicates DDD for

**C** (combination drugs, 1 tablet = 1 DDD)

**E** (drugs for external use, 1 gram = 1 DDD)

DDD indicated for pharmaceuticals for external use and combined products is not based on the amount of an active substance and can therefore not be compared to the DDD for other drugs.

**VOLUME IN DDD,**  
The sales by prescriptions and to hospitals in DDD (Defined Daily Doses) of the substance in Stockholm County Council during one year.  
(Sep 2012–Aug 2013)

## Substances which are Exempt from Classification

The use of some pharmaceuticals in the groups vitamins, electrolytes, amino acids, peptides, proteins, carbohydrates, lipids, vaccines and drugs based on herbs are not considered as a risk to the environment. That is the reason why these substances have not been assigned environmental information even though they are listed on the website [www.janusinfo.se/environment](http://www.janusinfo.se/environment). In this folder these substances are only presented if they are recommended in the Wise List (Kloka Listan). The assessment is then expressed as "exempt".

## The Precautionary Principle

According to the Precautionary Principle, measures can be taken if there is reason to believe that a product or a method of production involves unacceptable risks to the health of human beings, animals, plants and the environment – even if there is no definitive scientific proof of such an effect. The precautionary principle is a part of EU law and is valid in all member countries.

SUBSTANCE	RISK	P	B	T	VOLUME IN DDD
<b>A Alimentary Tract and Metabolism</b>					
<b>Stomatological preparations</b>					
triamcinolone	insignificant	4*	3	0	1*
					165 311
					<b>E -</b>
chlorhexidine	cannot be excl	6*	3*0	3*	-
					275 263
benzydamine	cannot be excl	-	-	-	-
<b>Drugs for acid-related disorders</b>					
<b>sodium bicarbonate</b>	exempt				
esomeprazole	insignificant	1*	0	0	1*
					4 046 556
					<b>C 78 848</b>
<b>omeprazole</b>	insignificant	1*	0	0	1*
<b>ranitidine</b>	insignificant	3	3	0	0
pantoprazole	insignificant	4	3	0	1
<b>misoprostol</b>	insignificant	4*	3*0	1	33 500
					505 350
rabeprazole	insignificant	5*	3*0	2	2 954
<b>clarithromycin</b>	insignificant	6	3	0	3
					59 076
					<b>C 17 248</b>
lansoprazole	cannot be excl	4	3	0	1
glycopyrronium	cannot be excl	-	-	0	-
					2 931
					<b>C 22 010</b>
alginic acid	cannot be excl	-	-	-	-
dimethicone	cannot be excl	-	-	-	-
					1 578 953
					<b>C 840</b>
papaverine	cannot be excl	-	-	-	-
					413 560
					<b>C 8 600</b>
<b>Drugs for functional gastrointestinal disorders</b>					
butylscopolamine	insignificant	4	3	0	1
					7 254
atropine	cannot be excl	-	-	0	-
					25 068
					<b>C -</b>
<b>metoclopramide</b>	cannot be excl	-	-	0	-
hyoscyamine	cannot be excl	-	-	-	-
					109 866
<b>Antiemetics and antinauseants</b>					
gransetron	insignificant	4	3	0	1
					4 583
aprepitant	insignificant	6*	3	0	3*
scopolamine	cannot be excl	-	-	0	-
					8 600
palonosetron	cannot be excl	-	-	-	-
					1 055
<b>ondansetron</b>		6	3	0	3
tropisetron		9*	3	3*	3
					40

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>Drugs for constipation</b>						
<b>psyllium</b>	exempt					
<b>lactulose</b>	exempt					
<b>macrogol</b>	exempt					
<b>sodium picosulfate</b>	exempt					
<b>karaya gum</b>	exempt					
bisacodyl	insignificant	5	3	0	2	121 282
docusate sodium	cannot be excl	8*	3*3	2*		<b>C-</b>
sodium sulphate	cannot be excl	-	-	-	-	<b>C -</b>
ursodeoxycholic acid	cannot be excl					392 973
<b>Antidiarrheals, intestinal antiinflammatory/antiinfective agents</b>						
<b>budesonide</b>	insignificant	5	3	0	2	8 079 288
						<b>C 8 099 610</b>
<b>loperamide</b>	insignificant	7*	3*3	1		855 503
						<b>C 840</b>
sodium cromoglycate	cannot be excl	3*	3*0	0*		103 116
olsalazine	cannot be excl	3*	3*0	0		69 452
<b>mesalazine</b>	cannot be excl	6*	3	0	3*	2 128 687
<b>prednisolone</b>	cannot be excl	-	-	0	-	5 381 008
						<b>E -</b>
dimethicone	cannot be excl	-	-	-	-	1 578 953
						<b>C 840</b>
<b>nystatin</b>	cannot be excl	-	-	-	-	165 723
sulfasalazine	cannot be excl	-	-	-	-	710 974
<b>Antiobesity preparations, excl diet products</b>						
orlistat	insignificant	8	3	3	2	438 788
sibutramine	cannot be excl	6	3	0	3	-
<b>Drugs used in diabetes</b>						
<b>insulin</b>	exempt					
<b>liraglutide</b>	exempt					
saxagliptin	insignificant	2*	0	0	2*	58 765
						<b>C -</b>
<b>glibenclamide</b>	insignificant	3	3	0	0	1 660 466
<b>metformin</b>	insignificant	4	3	0	1	11 758 820
						<b>C 190 666</b>
vildagliptin	insignificant	4*	3	0	1*	7 665
						<b>C 6 930</b>
sitagliptin	insignificant	5	3	0	2	882 526
						<b>C 178 416</b>
<b>glimepiride</b>	insignificant	6*	3	3*	0	1 825 222
acarbose	cannot be excl	3	3	0	0	43 203
<b>glipizide</b>	cannot be excl	4*	3*0	1*		298 780

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>repaglinide</b>	cannot be excl	4*	3	0	1*	335 764
<b>pioglitazone</b>	cannot be excl	-	-	-	-	172 215
						<b>C 5 320</b>
<b>Vitamins</b>						
<b>alfacalcidol</b>	exempt					
<b>colecalciferol</b>	exempt					
<b>Mineral supplements</b>						
<b>calcium carbonate</b>	exempt					
<b>potassium chloride</b>	exempt					
<b>Anabolic agents for systemic use</b>						
<b>nandrolone</b>	cannot be excl	-	-	-	-	75
<b>B Blood and Blood-Forming Organs</b>						
<b>Antithrombotic agents</b>						
<b>alteplase</b>	exempt					
<b>dalteparin</b>	exempt					
<b>enoxaparin</b>	exempt					
<b>heparin sodium</b>	exempt					
<b>tinzaparin</b>	exempt					
prasugrel	insignificant	2	0	0	2	22 974
<b>ticagrelor</b>	insignificant	2	0	0	2	268 702
dabigatran	insignificant	2*	0	0	2*	662 728
tirofiban	insignificant	3	3	0	0	170
<b>warfarin</b>	insignificant	4	3	0	1	7 027 345
<b>rivaroxaban</b>	insignificant	6*	3	0	3*	503 951
argatroban	insignificant	7*	3	3*	1	205
<b>clopidogrel</b>	insignificant	8	3	3	2	3 306 532
<b>dipyridamole</b>	low	8	3	3	2	1 372 650
						<b>C 253 920</b>
iloprost	cannot be excl	1*	0	0	1*	1 575
ticlopidine	cannot be excl	6*	3*0	3		2 600
<b>fondaparinux</b>	cannot be excl	6*	3*0	3*		12 188
eftibatide	cannot be excl	-	-	0	-	6
<b>acetylsalicylic acid</b>	cannot be excl	-	-	-	-	38 231 279
						<b>C 6 573 994</b>
<b>Antihemorrhagics</b>						
<b>phytomenadione</b>	exempt					
<b>tranexamic acid</b>	exempt					
<b>Antianemic preparations</b>						
<b>cyanocobalamin</b>	exempt					
<b>darbepoetin alfa</b>	exempt					

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>ferric carboxy-maltose</b>	exempt					
<b>epoetin zeta</b>	exempt					
<b>ferrous glycine sulfate</b>	exempt					
<b>folic acid</b>	exempt					
<b>iron 2<sup>+</sup> and 3<sup>+</sup></b>	exempt					
<b>Blood substitutes and perfusion solutions</b>						
<b>alanyl glutamine</b>	exempt					
<b>potassium chloride</b>	exempt					
<b>sodium glycerophosphate</b>	exempt					

## C Cardiovascular System

### Cardiac therapy

<b>lidocaine</b>	insignificant	3	3	0	0	24
		<b>C, E 431 819</b>				
<b>glyceryl trinitrate</b>	insignificant	6	3	0	3	1 403 569
		<b>E -</b>				
<b>dronedarone</b>	low	6	3	0	3	140 950
<b>disopyramide</b>	cannot be excl	4*	3*0	1*		145 395
<b>isosorbide mononitrate</b>	cannot be excl	4*	3*0	1*		6 679 049
<b>milrinone</b>	cannot be excl	4*	3	0	1*	482
<b>amiodarone</b>	cannot be excl	7*	3	3	1*	173 333
<b>etilefrine</b>	cannot be excl	8*	3	3*	2*	44 350
<b>epinephrine</b>	cannot be excl	-	-	0	-	155 304
		<b>C -</b>				
<b>vernakalant</b>	cannot be excl	-	-	0	-	23
<b>alprostadil</b>	cannot be excl	-	-	-	-	162 937
<b>digoxin</b>	cannot be excl	-	-	-	-	1 725 731
<b>dopamine</b>	cannot be excl	-	-	-	-	584
<b>flecainide</b>	cannot be excl	-	-	-	-	306 185
<b>norepinephrine</b>	cannot be excl	-	-	-	-	29 895

### Antihypertensives

<b>moxonidine</b>	insignificant	5	3	0	2	87 579
<b>hydralazine</b>	cannot be excl	6*	3	0	3*	3 750
<b>doxazosin</b>	cannot be excl	6*	3	0	3*	1 296 763
<b>clonidine</b>	cannot be excl	6*	3	0	3*	37 163
<b>bosentan</b>	cannot be excl	-	-	0	-	19 012

### Diuretics

<b>torasemide</b>	insignificant	4	3	0	1	68 850
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SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>furosemide</b>	insignificant	4	3	0	1	21 575 294
<b>hydrochlorthiazide</b>	insignificant	4*	3	0	1*	2 830 612
		<b>C 24 086 325</b>				
<b>eplerenone</b>	insignificant	6	3	0	3	104 450
<b>bendroflumethiazide</b>	cannot be excl	4*	3*0	1		5 349 201
		<b>C 193 113</b>				
<b>bumetanide</b>	cannot be excl	4*	3*0	1		66 772
<b>amiloride</b>	cannot be excl	4*	3*0	1*		265 945
		<b>C 7 708 633</b>				
<b>metolazone</b>	cannot be excl	-	-	-	-	17 650
<b>spironolactone</b>	cannot be excl	-	-	-	-	2 079 512
<b>Vasoprotectives</b>						
<b>lidocaine</b>	insignificant	3	3	0	0	24
		<b>C, E 431 819</b>				
<b>glucosamine</b>	cannot be excl	1	0	0	1	749 537
		<b>U -</b>				
<b>hydrocortisone</b>	cannot be excl	-	-	0	-	401 062
		<b>C, E -</b>				
<b>framycetin</b>	cannot be excl	-	-	0	-	<b>E -</b>
<b>prednisolone</b>	cannot be excl	-	-	0	-	5 381 008
		<b>E -</b>				
<b>cincocaine</b>	cannot be excl	-	-	3	-	<b>E -</b>
<b>sodium oleate</b>	cannot be excl	-	-	-	-	-
<b>Beta-blocking agents</b>						
<b>bisoprolol</b>	insignificant	4	3	0	1	4 596 898
<b>pindolol</b>	insignificant	4	3	0	1	85 505
<b>carvedilol</b>	insignificant	6	3	0	3	699 922
<b>metoprolol</b>	low	4	3	0	1	18 920 983
		<b>C 462 238</b>				
<b>propranolol</b>	moderate	3	0	0	3	1 217 783
<b>atenolol</b>	cannot be excl	4*	3*0	1*		3 820 508
<b>labetalol</b>	cannot be excl	6*	3*0	3*		49 187
<b>sotalol</b>	cannot be excl	6*	3	0	3*	684 450
<b>esmolol</b>	cannot be excl	-	-	-	-	21
<b>Calcium-channel blockers</b>						
<b>amlodipine</b>	insignificant	6	3	0	3	31 233 736
		<b>C 87 024</b>				
<b>isradipine</b>	insignificant	9	3	3	3	151 150
<b>felodipine</b>	low	9	3	3	3	13 326 881
		<b>C 462 238</b>				
<b>diltiazem</b>	cannot be excl	4*	3	0	1*	652 285
<b>verapamil</b>	cannot be excl	4*	3*0	1*		667 772

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
nifedipine	cannot be excl	5*	3	0	2*	264 469
lercanidipine	cannot be excl	-	-	-	-	295 066
<b>Agents acting on the renin-angiotensin system</b>						
<b>losartan</b>	insignificant	3	3	0	0	12 784 091 <b>C 5 444 709</b>
eprosartan	insignificant	4	3	0	1	55 678 <b>C 41 188</b>
irbesartan	insignificant	4	3	0	1	1 689 855 <b>C 826 588</b>
valsartan	insignificant	4	3	0	1	1 670 083 <b>C 1 090 324</b>
<b>candesartan</b>	insignificant	4*	3	0	1*	19 576 160 <b>C 3 630 730</b>
fosinopril	insignificant	4*	3	0	1*	3 200
telmisartan	insignificant	5	3	0	2	370 909 <b>C 149 842</b>
<b>ramipril</b>	insignificant	6*	3	3*	0	17 748 627 <b>C 238 282</b>
<b>enalapril</b>	cannot be excl	3*	3	0	0*	33 105 589 <b>C 4 883 561</b>
lisinopril	cannot be excl	3*	3	0	0*	802 941 <b>C 83 276</b>
captopril	cannot be excl	4*	3	0	1*	299 534
quinapril	cannot be excl	-	-	-	-	50 340 <b>C 76 216</b>
<b>Lipid-modifying agents</b>						
rosuvastatin	insignificant	1	0	0	1	3 888 335
fenofibrate	insignificant	3	3	0	0	146 130
<b>atorvastatin</b>	insignificant	4	3	0	1	8 097 305
fluvastatin	insignificant	4	3	0	1	12 712
pravastatin	insignificant	4	3	0	1	897 476
bezafibrate	insignificant	5	3	0	2	97 342
ezetimibe	insignificant	6	3	0	3	1 498 336 <b>C 101 850</b>
<b>simvastatin</b>	low	4	3	0	1	31 493 813 <b>C 101 850</b>
gemfibrozil	low	5	3	0	2	233 259
<b>cholestyramine</b>	cannot be excl	6*	3	0	3*	102 516
colestipol	cannot be excl	-	-	-	-	26 960

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>D Dermatologicals</b>						
<b>Antifungals for dermatological use</b>						
<b>clotrimazole</b>	insignificant	9	3	3	3	<b>E 18 857</b>
<b>ketoconazole</b>	low	6*	3	0*	3	13 820 <b>E -</b>
econazole	low	-	-	-	3	<b>E 10 544</b>
<b>miconazole</b>	cannot be excl	9	3	3	3	64 <b>E -</b>
<b>terbinafine</b>	cannot be excl	9*	3*	3	3	521 948 <b>E -</b>
bifonazole	cannot be excl	-	-	-	-	<b>E -</b>
<b>Emollients and protectives</b>						
<b>glycerin</b>	exempt					
<b>propylene glycol</b>	exempt					
<b>urea</b>	exempt					
<b>Antipruritics incl antihistamines, anesthetics, etc</b>						
lidocaine	insignificant	3	3	0	0	24 <b>C, E 431 819</b>
<b>Antipsoriatics</b>						
<b>calcipotriol</b>	cannot be excl	9*	3	3	3*	<b>E -</b>
acitretin		9	3	3	3	67 242
<b>Antibiotics and chemotherapeutics for dermatological use</b>						
penciclovir	insignificant	3*	3	0	0*	<b>E -</b>
aciclovir	insignificant	4	3	0	1	95 121 <b>E -</b>
mupirocin	cannot be excl	3*	3*	0	0*	<b>E -</b>
<b>retapamulin</b>	cannot be excl	5*	3	0	2*	<b>E -</b>
gentamicin	cannot be excl	6	3	0	3	12 873 <b>E -</b>
fusidic acid	cannot be excl	6*	3	0	3*	5 493 <b>E -</b>
<b>metronidazole</b>	cannot be excl	6*	3	0	3*	203 434 <b>E 24 545</b>
oxytetracycline	cannot be excl	6*	3*	0	3*	<b>-</b> <b>C, E -</b>
<b>imiquimod</b>	cannot be excl	-	-	-	-	<b>-</b>
<b>podophyllotoxin</b>	cannot be excl	-	-	-	-	<b>E -</b>
<b>Corticosteroids, dermatological preparations</b>						
triamcinolone	insignificant	4*	3	0	1*	165 311 <b>E -</b>
clobetasol	insignificant	9*	3	3	3*	<b>E -</b>

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>mometasone</b>	low	5	3	0	2	9 459 810 E -
fluticasone	cannot be excl	6	3	0	3	2 294 110 <b>C, E</b> 11 002 800
<b>clobetasone</b>	cannot be excl	9	3	3	3	E -
<b>betamethasone</b>	cannot be excl	9*	3	3*	3*	2 507 905 E -
<b>hydrocortisone</b>	cannot be excl	-	-	0	-	401 062 <b>C, E</b> -
fluocinolone	cannot be excl	-	-	-	-	E -
<b>Antiseptics and disinfectants</b>						
chlorhexidine	cannot be excl	6*	3*	0	3*	- E 275 263
<b>Anti-acne preparations</b>						
<b>benzoyl peroxide</b>	moderate	3	0	0	3	E -
clindamycin	cannot be excl	6*	3	0	3*	254 308 E 55 367
<b>adapalene</b>	cannot be excl	-	-	-	-	E -
<b>azelaic acid</b>	cannot be excl	-	-	-	-	E -
tretinoin	cannot be excl	-	-	-	-	E -
<b>Other dermatological preparations</b>						
finasteride	insignificant	7	3	3	1	4 107 958
salicylic acid	cannot be excl	4*	3*	0	1*	E -
<b>pimecrolimus</b>	cannot be excl	7*	3	3*	1*	E -
minoxidil	cannot be excl	-	-	-	-	E -
selenium sulfide	cannot be excl	-	-	-	-	E -
<b>tacrolimus</b>	cannot be excl	-	-	-	-	342 035

G Genito-Urinary System and Sex Hormones						
Gynecological anti-infectives and antiseptics						
<b>clotrimazole</b>	insignificant	9	3	3	3	E 18 857
econazole	low	-	-	-	3	E 10 544
<b>clindamycin</b>	cannot be excl	6*	3	0	3*	254 308 E 55 367
<b>metronidazole</b>	cannot be excl	6*	3	0	3*	203 434 E 24 545
Other gynecologicals						
<b>etonogestrel</b>	insignificant	6*	3	0	3*	4 749 000 E -
<b>ethinylestradiol</b>	high	9	3	3	3	E 20 466 535
<b>methylergometrine</b>	cannot be excl	7*	3	3*	1*	11 270

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>atosiban</b>	cannot be excl	-	-	-	-	368
<b>dinoprostone</b>	cannot be excl	-	-	-	-	6 772
<b>cabergoline</b>	cannot be excl	-	-	-	-	21 492
<b>carboprost</b>	cannot be excl	-	-	-	-	55
gemeprost	cannot be excl	-	-	-	-	55
quinagolide	cannot be excl	-	-	-	-	59 190
<b>bromocriptine</b>	9*	3	3*	3	-	130 929
<b>Sex hormones and modulators of the genital system</b>						
<b>corionic gonado-</b>	exempt					
<b>trophin</b>						
dienogest	insignificant	4	3	0	1	19 348 C -
<b>desogestrel</b>	insignificant	5	3	0	2	8 718 819 C 744 072
<b>drospirenone</b>	insignificant	5	3	0	2	<b>C</b> 5 566 680
<b>etonogestrel</b>	insignificant	6*	3	0	3*	4 749 000 E -
<b>nomegestrol</b>	insignificant	6*	3	0	3*	<b>C</b> 835 548
dydrogesterone	insignificant	8	3	3	2	-
<b>estradiol</b>	moderate	9	3	3	3	4 886 028 C 3 834 979
<b>ethinylestradiol</b>	high	9	3	3	3	<b>C</b> 20 466 535 E -
testosterone	cannot be excl	3	0	0	3	1 347 658
<b>estriol</b>	cannot be excl	6*	3*	0	3*	1 717 834
raloxifene	cannot be excl	8	3	3	2	131 632
<b>norethisterone</b>	cannot be excl	9	3	3	3	1 115 762 C 2 901 018
ciproterone	cannot be excl	9*	3	3	3*	30 580 C 711 480
<b>levonorgestrel</b>	cannot be excl	9*	3	3	3*	1 730 <b>C</b> 10 129 784
tibolone	cannot be excl	-	-	0	-	982 632
lynestrenol	cannot be excl	-	-	3	-	976 291 C 21 971
<b>ulipristal</b>	cannot be excl	-	-	3	-	6 249
<b>clomiphene</b>	cannot be excl	-	-	-	-	192 849
<b>medroxy-</b>	cannot be excl	-	-	-	-	1 562 582
<b>progesterone</b>	cannot be excl	-	-	-	-	<b>C</b> 1 038 989
<b>mifepristone</b>	cannot be excl	-	-	-	-	3 061
norgestimate	cannot be excl	-	-	-	-	<b>C</b> 2 351 972
<b>progesterone</b>	cannot be excl	-	-	-	-	E 1 197 023

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>Urologicals</b>						
<b>sildenafil</b>	insignificant	2	0	0	2	559 030
fesoterodine	insignificant	2*	0	0	2*	501 965
<b>alfuzosin</b>	insignificant	4*	3*0	1		6 175 552
<b>tadalafil</b>	insignificant	5	3	0	2	643 075
darifenacin	insignificant	6	3	0	3	160 384
<b>finasteride</b>	insignificant	7	3	3	1	4 107 958
terazosin	cannot be excl	6*	3	0	3*	476 340
<b>tolterodine</b>	cannot be excl	6*	3*0	3*		944 398
dutasteride	cannot be excl	8*	3	3	2*	76 440
vardenafil	cannot be excl	9*	3	3	3*	54 014
solifenacain	cannot be excl	-	-	0	-	2 322 832
<b>alprostadil</b>	cannot be excl	-	-	-	-	162 937
oxybutynin	cannot be excl	-	-	-	-	187 323

## H Systemic Hormonal Preparations excl Sex Hormones and Insulins

Pituitary and hypothalamic hormones and analogues						
<b>desmopressin</b>	exempt					
<b>ganirelix</b>	exempt					
<b>nafarelin</b>	exempt					
<b>oxytocin</b>	exempt					
Corticosteroids for systemic use						
<b>triamcinolone</b>	insignificant	4*	3	0	1*	165 311
		<b>E -</b>				
<b>betamethasone</b>	cannot be excl	9*	3	3*	3*	2 507 905
		<b>E -</b>				
dexamethasone	cannot be excl	-	-	0	-	38 441
		<b>C -</b>				
<b>hydrocortisone</b>	cannot be excl	-	-	0	-	401 062
		<b>C, E -</b>				
<b>prednisolone</b>	cannot be excl	-	-	0	-	5 381 008
		<b>E -</b>				
prednisone	cannot be excl	-	-	0	-	351 413
<b>fludrocortisone</b>	cannot be excl	-	-	-	-	327 900
<b>methylprednisolone</b>	cannot be excl	-	-	-	-	431 819
Thyroid therapy						
<b>levothyroxine</b>	cannot be excl	-	-	-	-	19 477 059
liothyronine	cannot be excl	-	-	-	-	100 190
<b>thiamazole</b>	cannot be excl	-	-	-	-	646 730
Pancreatic Hormones						
<b>glucagon</b>	exempt					

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>Calcium homeostasis</b>						
<b>cincalcet</b>	insignificant	6	3	0	3	67 205
<b>J Anti-Infectives for Systemic Use</b>						
<b>Antibacterials for systemic use</b>						
<b>trimethoprim</b>	insignificant	4	3	0	1	149 661
		<b>C 261 420</b>				
<b>nitrofurantoin</b>	insignificant	5	3	0	2	279 144
<b>erythromycin</b>	insignificant	6	3	0	3	133 025
clarithromycin	insignificant	6	3	0	3	59 076
		<b>C 17 248</b>				
<b>meropenem</b>	insignificant	6	3	0	3	40 051
telithromycin	insignificant	9	3	3	3	10
ofloxacin	insignificant	9*	3	3*	3	1 580
azitromycin	low	6	3	0	3	86 066
<b>ceftazidime</b>	low	6	3	0	3	3 229
<b>pivmecillinam</b>	low	6	3	0	3	474 053
<b>sulfamethoxazole</b>	low	6	3	0	3	261 420
tetracycline	low	6	3	0	3	118 944
<b>amoxicillin</b>	moderate	6	3	0	3	953 571
		<b>C 272 984</b>				
<b>ciprofloxacin</b>	moderate	6	3	0	3	617 156
		<b>E -</b>				
<b>gentamicin</b>	cannot be excl	6	3	0	3	12 873
		<b>E -</b>				
<b>ampicillin</b>	cannot be excl	6*	3	0	3*	14 355
aztreonam	cannot be excl	6*	3*0	3		353
<b>benzylpenicillin</b>	cannot be excl	6*	3	0	3*	39 307
cefuroxime	cannot be excl	6*	3	0	3*	13 381
ceftibuten	cannot be excl	6*	3*0	3*		27 125
ceftriaxone	cannot be excl	6*	3	0	3*	12 987
		<b>C -</b>				
<b>cloxacillin</b>	cannot be excl	6*	3	0	3*	110 145
<b>clindamycin</b>	cannot be excl	6*	3	0	3*	254 308
		<b>E 55 367</b>				
ertapenem	cannot be excl	6*	3	0	3*	2 556
fusidic acid	cannot be excl	6*	3	0	3*	5 493
		<b>E -</b>				
<b>imipenem</b>	cannot be excl	6*	3	0	3*	7 164
cilastatin	cannot be excl	5*	3	0	2*	
(enzyme inhibitor)						
<b>metronidazole</b>	cannot be excl	6*	3	0	3*	203 434
		<b>E 24 545</b>				

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
moxifloxacin	cannot be excl	6*	3	0	3*	13 481
oxytetracycline	cannot be excl	6*	3*0	3*	-	C, E -
<b>cefotaxime</b>	cannot be excl	9*	3	3*	3*	58 771
daptomycin	cannot be excl	-	-	0	-	149
<b>flucloxacillin</b>	cannot be excl	-	-	0	-	1 453 923
<b>phenoxycephalothin-</b>	cannot be excl	-	-	0	-	3 256 728
<b>penicillin</b>	cannot be excl	-	-	0	-	C -
tobramycin	cannot be excl	-	-	0	-	7 113
roxithromycin	cannot be excl	-	-	-	1*	2 250
norfloxacin	cannot be excl	-	-	-	3	20 850
amikacin	cannot be excl	-	-	-	-	1 853
<b>cefadroxil</b>	cannot be excl	-	-	-	-	93 639
cefalexin	cannot be excl	-	-	-	-	1 404
<b>doxycycline</b>	cannot be excl	-	-	-	-	1 389 103
levofloxacin	cannot be excl	-	-	-	-	22 171
linezolid	cannot be excl	-	-	-	-	3 275
<b>lumecycline</b>	cannot be excl	-	-	-	-	1 176 099
methenamine	cannot be excl	-	-	-	-	1 235 894
netilmicin	cannot be excl	-	-	-	-	-
<b>piperacillin</b>	cannot be excl	-	-	-	-	43 488
tazobactam (enzyme inhibitor)	cannot be excl	-	-	-	-	E -
<b>Antimycotics for systemic use</b>						
caspofungin	insignificant	6	3	0	3	2 770
itraconazole	insignificant	6	3	3	0	18 936
posaconazole	insignificant	9	3	3	3	9 361
ketoconazole	low	6*	3	0*	3	13 820
<b>fluconazole</b>	cannot be excl	4*	3*0	1	-	187 903
amphotericin B	cannot be excl	-	-	-	-	4 917
flucytocine	cannot be excl	-	-	-	-	4
voriconazole	cannot be excl	-	-	-	-	4 895
<b>Antimycobacterials</b>						
isoniazid	insignificant	4	3	0	1	133 480
rifampicin	cannot be excl	-	-	-	0*	87 490
rifabutin	cannot be excl	-	-	-	-	3 570
<b>Antivirals for systemic use</b>						
stavudine	insignificant	1	0	0	1	378
indinavir	insignificant	1*	0	0	1*	30

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
boceprevir	insignificant	2*	0	0	2*	2 184
famciclovir	insignificant	3	3	0	0	5 857
fosamprenavir	insignificant	3	3	0	0	270
foscarinet	insignificant	3	3	0	0	-
ganciclovir	insignificant	3	3	0	0	872
valganciclovir	insignificant	3	3	0	0	20 335
didanosine	insignificant	3*	3	0	0*	881
abacavir	insignificant	4	3	0	1	11 350
						<b>C 366 450</b>
<b>aciclovir</b>	insignificant	4	3	0	1	95 121
						<b>E -</b>
entecavir	insignificant	4	3	0	1	44 640
lamivudine	insignificant	4	3	0	1	46 088
						<b>C 371 640</b>
nevirapine	insignificant	4	3	0	1	61 849
ribavirin	insignificant	4	3	0	1	31 629
<b>valaciclovir</b>	insignificant	4	3	0	1	312 871
oseltamivir	insignificant	4*	3	0	1*	6 570
atazanavir	insignificant	5	3	0	2	217 040
tipranavir	insignificant	5	3	0	2	-
darunavir	insignificant	5*	3	0	2*	120 360
efavirenz	insignificant	6	3	0	3	117 517
						<b>C 176 460</b>
etravirine	insignificant	6	3	0	3	43 770
telaprevir	insignificant	6*	3	0	3*	4 312
saquinavir	insignificant	7	3	3	1	767
zanamivir	cannot be excl	3*	3	0	0*	205
zidovudine	cannot be excl	4*	3	0	1*	4 429
						<b>C 8 520</b>
<b>Immune sera and immunoglobulins</b>						
<b>immunoglobulin</b>	exempt					
<b>anti-d</b>						
<b>L Antineoplastic and Immunomodulating Agents</b>						
<b>Antineoplastic agents</b>						
pemetrexed	insignificant	1	0	0	1	-
temozolamide	insignificant	1	0	0	1	-
erlotinib	insignificant	3	3	0	0	-
hydroxycarbamide	insignificant	3	3	0	0	-
nelarabine	insignificant	3	3	0	0	-
gemcitabine	insignificant	5	3	0	2	-
imatinib	insignificant	5	3	0	2	-

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
gefitinib	insignificant	5*	3	0	2*	-
cladribine	insignificant	5*	3*	0	2	-
capecitabine	insignificant	6	3	0	3	-
sunitinib	insignificant	6*	3*	0	3	-
cabazitaxel	insignificant	9	3	3	3	-
nilotinib	insignificant	9	3	3	3	-
dasatinib	insignificant	9*	3	3	3*	-
bortezomib	insignificant	-	-	-	3	-
sorafenib	low	9	3	3	3	-
topotecan	cannot be excl	1*	0	0	1*	-
busulfan	cannot be excl	2*	0	0	2*	-
chlorambucil	cannot be excl	2*	0	0	2*	-
melphalan	cannot be excl	2*	0	0	2*	-
etoposide	cannot be excl	3*	3*	0	0*	-
carboplatin	cannot be excl	4*	3*	0	1*	-
mercaptopurine	cannot be excl	4*	3	0	1*	-
cyclophosphamide	cannot be excl	5	3	0	2	-
mitomycin	cannot be excl	6	3	0	3	-
tioguanine	cannot be excl	6	3	0	3	-
cisplatin	cannot be excl	6*	3*	0	3	-
ifosfamide	cannot be excl	6*	3	0	3*	-
methyl aminolevulinate	cannot be excl	6*	3	0	3*	-
oxaliplatin	cannot be excl	6*	3	0	3*	-
paclitaxel	cannot be excl	6*	0	3	3*	-
docetaxel	cannot be excl	9*	3	3*	3*	-
doxorubicin	cannot be excl	-	-	-	2*	-
aminolevulinic acid	cannot be excl	-	-	-	-	-
amsacrine	cannot be excl	-	-	-	-	-
anagrelide	cannot be excl	-	-	-	-	-
bexarotene	cannot be excl	-	-	-	-	-
bleomycin	cannot be excl	-	-	-	-	-
brentuximab vedotin	cannot be excl	-	-	-	-	-
clofarabine	cannot be excl	-	-	-	-	-
cytarabine	cannot be excl	-	-	-	-	-
dacarbazine	cannot be excl	-	-	-	-	-
daunorubicin	cannot be excl	-	-	-	-	-
epirubicin	cannot be excl	-	-	-	-	-
estramustine	cannot be excl	-	-	-	-	-
fludarabine	cannot be excl	-	-	-	-	-
fluorouracil	cannot be excl	-	-	-	-	-
idarubicin	cannot be excl	-	-	-	-	-
irinotecan	cannot be excl	-	-	-	-	-
lomustine	cannot be excl	-	-	-	-	-
miltefosine	cannot be excl	-	-	-	-	-

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
mitoxantrone	cannot be excl	-	-	-	-	-
pixantrone	cannot be excl	-	-	-	-	-
trabectedin	cannot be excl	-	-	-	-	-
vinblastine	cannot be excl	-	-	-	-	-
vincristine	cannot be excl	-	-	-	-	-
vindesine	cannot be excl	-	-	-	-	-
vinflunine	cannot be excl	-	-	-	-	-
vinorelbine	cannot be excl	-	-	-	-	-
<b>Endocrine therapy</b>						
<b>leuprorelin</b>	exempt					
letrozole	insignificant	4	3	0	1	332 920
<b>anastrozole</b>	insignificant	5*	3	0	2*	803 642
<b>tamoxifen</b>	insignificant	6	3	0	3	1 197 292
<b>bicalutamide</b>	insignificant	6*	3	0	3*	1 324 215
abiraterone	low	3	0	0	3	10 560
fulvestrant	low	3*	0	0	3*	29 939
flutamide	cannot be excl	-	-	0	-	29 288
exemestane	cannot be excl	-	-	-	-	67 830
medroxyprogesterone	cannot be excl	-	-	-	-	1 562 582
						<b>C 1 038 989</b>
megestrol		9	3	3	3	30
<b>Immunostimulants</b>						
mifamurtide	cannot be excl	-	-	-	-	-
<b>Immunosuppressants</b>						
<b>adalimumab</b>	exempt					
<b>golimumab</b>	exempt					
<b>infliximab</b>	exempt					
ciclosporine	insignificant	4	0	3	1	131 246
leflunomide	insignificant	5	3	0	2	77 620
everolimus	insignificant	8	3	3	2	23 756
mycophenolic acid	moderate	6	3	0	3	213 572
<b>azathioprine</b>	cannot be excl	-	-	-	-	742 446
<b>methotrexate</b>	cannot be excl	-	-	-	-	2 221 070
tacrolimus	cannot be excl	-	-	-	-	342 035

## M Musculo-Skeletal System

### Antiinflammatory and antirheumatic products

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>ketorolac</b>	insignificant	4	3	0	1	23 370
meloxicam	insignificant	4	3	0	1	53 560
etoricoxib	insignificant	4*	3	0	1*	2 043 1766
misoprostol	insignificant	4*	3*	0	1	33 500
						<b>C 505 350</b>

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>naproxen</b>	low	4	3	0	1	7 744 751
dexibuprofen	low	5	3	0	2	192 823
glucosamine	cannot be excl	1	0	0	1	749 537
<b>ketoprofen</b>	cannot be excl	4*	3	0	1*	1 967 496
						<b>E -</b>
indometacin	cannot be excl	5*	3	0	2*	14 138
diclofenac	cannot be excl	-	3	-	-	4 412 946
						<b>C, E 624 897</b>
auranofin	cannot be excl	-	-	-	-	3 850
<b>ibuprofen</b>	cannot be excl	-	-	-	-	2 189 840
						<b>E 16 450</b>
lornoxicam	cannot be excl	-	-	-	-	11 170
nabumetone	cannot be excl	-	-	-	-	314 865
piroxicam	cannot be excl	-	-	-	-	69 180
sodium aurothiomalate	cannot be excl	-	-	-	-	2 083
sulindac	cannot be excl	-	-	-	-	-
tenoxicam		4	3	0	1	68 556
<b>Topical products for joint and muscular pain</b>						
diethylaminosalicylate	cannot be excl	1*	0	0	1*	<b>E 321</b>
<b>ketoprofen</b>	cannot be excl	4*	3	0	1*	1 967 496
						<b>E 1 467 985</b>
<b>ibuprofen</b>	cannot be excl	-	-	-	-	2 189 840
						<b>E 16 450</b>
<b>Muscle relaxants</b>						
atracurium	cannot be excl	2*	0	0	2*	-
cisatracurium	cannot be excl	2*	0	0	2*	-
baclofen	cannot be excl	3*	3	0	0*	400 216
mivacurium	cannot be excl	3*	3	0	0*	-
orphenadrine	cannot be excl	-	-	0	-	78 153
						<b>C 112 805</b>
rocuronium	cannot be excl	-	-	0	-	-
chlorzoxazone	cannot be excl	-	-	-	-	396 965
suxamethonium	cannot be excl	-	-	-	-	-
<b>Antigout preparations</b>						
<b>allopurinol</b>	cannot be excl	6	3	0	3	1 747 779
probencid	cannot be excl	-	-	-	-	82 000
<b>Drugs for treatment of bone diseases</b>						
<b>calcium carbonate</b>	exempt					
<b>denosumab</b>	exempt					
ibandronic acid	insignificant	2	0	0	2	507 107
clodronic acid	insignificant	4	3	0	1	4 802
<b>alendronic acid</b>	insignificant	4*	3	0	1*	3 589 579
						<b>C 85 960</b>

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>pamidronic acid</b>	insignificant	4*	3*	0	1*	4 305
etidronic acid	insignificant	5	3	0	2	-
						<b>C 2 240</b>
<b>zoledronic acid</b>	insignificant	5*	3	0	2*	2 404
risedronic acid	insignificant	6*	3*	0	3	608 384
						<b>C -</b>
<b>N Nervous System</b>						
<b>Anaesthetics</b>						
<b>lidocaine</b>	insignificant	3	3	0	0	24
						<b>C, E 431 819</b>
<b>prilocaine</b>	insignificant	4	3	0	1	-
						<b>C, E -</b>
ropivacaine	insignificant	4	3	0	1	-
propofol	low	6	3	0	3	-
fentanyl	cannot be excl	4	3	0	1	617 900
						excl inj liquid
mepivacaine	cannot be excl	4*	3*	0	1*	-
						<b>C 54 133</b>
remifentanil	cannot be excl	4*	3	0	1*	-
bupivacaine	cannot be excl	5*	3*	0	2*	-
						<b>C -</b>
<b>epinephrine</b>	cannot be excl	-	-	0	-	155 304
						<b>C -</b>
alfentanil	cannot be excl	-	-	-	-	-
capsaicin	cannot be excl	-	-	-	-	<b>E -</b>
desflurane	cannot be excl	-	-	-	-	-
<b>droperidol</b>	cannot be excl	-	-	-	-	12 400
isoflurane	cannot be excl	-	-	-	-	-
ketamine	cannot be excl	-	-	-	-	-
sufentanil	cannot be excl	-	-	-	-	-
thiopental	cannot be excl	-	-	-	-	-
<b>Analgesics</b>						
<b>naratriptan</b>	insignificant	3	3	0	0	7 164
<b>phenazone</b>	insignificant	3	3	0	0	<b>C 1 453</b>
<b>codeine</b>	insignificant	4	3	0	1	96 869
						<b>C 6 315 472</b>
rizatriptan	insignificant	4	3	0	1	235 176
<b>sumatriptan</b>	insignificant	4	3	0	1	896 620
<b>buprenorphine</b>	insignificant	6*	3	0	3*	806 130
						<b>C 210 964</b>
<b>paracetamol</b>	low	5	3	0	2	18 497 727
						<b>C 6 419 677</b>

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
ergotamine	low	7	3	3	1	<b>C 13 925</b>
<b>fentanyl</b>	cannot be excl	4	3	0	1	617 900
						excl inj liquid
zolmitriptan	cannot be excl	4*	3	0	1*	436 171
eletriptan	cannot be excl	5*	3*	0	2*	20 283
pizotifen	cannot be excl	9*	3	3	3*	16 565
scopolamine	cannot be excl	-	-	0	-	-
						<b>C 8 600</b>
<b>acetylsalicylic acid</b>	cannot be excl	-	-	-	-	38 231 279
						<b>C 6 573 994</b>
almotriptan	cannot be excl	-	-	-	-	13 623
<b>hydromorphone</b>	cannot be excl	-	-	-	-	241 755
						<b>C -</b>
ketobemidone	cannot be excl	-	-	-	-	86 047
						<b>C 15 764</b>
methylscopolamine	cannot be excl	-	-	-	-	<b>C 8 600</b>
<b>morphine</b>	cannot be excl	-	-	-	-	751 404
						<b>C 8 600</b>
<b>oxycodone</b>	cannot be excl	-	-	-	-	1 143 469
						<b>C 120 301</b>
papaverine	cannot be excl	-	-	-	-	413 560
						<b>C 8 600</b>
pethidine	cannot be excl	-	-	-	-	1 491
tramadol	cannot be excl	-	-	-	-	2 242 848
<b>Antiepileptics</b>						
zonisamide	insignificant	1	0	0	1	59 514
pregabalin	insignificant	3*	3	0	0*	2 305 710
<b>carbamazepine</b>	insignificant	4	3	0	1	1 167 875
<b>lamotrigine</b>	insignificant	4	3	0	1	1 408 020
clonazepam	insignificant	4*	3	0	1*	148 831
topiramate	insignificant	4*	3*	0	1	135 659
<b>valproic acid</b>	insignificant	4*	3	0	1*	1 147 930
retigabine	insignificant	6	3	0	3	1 440
felbamate	cannot be excl	4*	3	0	1*	210
<b>oxcarbazepine</b>	cannot be excl	4*	3	0	1*	117 990
vigabatrin	cannot be excl	4*	3*	0	1*	11 634
ethosuximide	cannot be excl	-	-	-	-	17 504
fosphenytoin	cannot be excl	-	-	-	-	6 385
<b> gabapentin</b>	cannot be excl	-	-	-	-	779 653
<b> levetiracetam</b>	cannot be excl	-	-	-	-	764 749
phenytoin	cannot be excl	-	-	-	-	414 313
<b>Anti-Parkinson drugs</b>						
<b>levodopa</b>	insignificant	2	0	0	2	<b>C 1 183 091</b>

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>pramipexole</b>	insignificant	4	3	0	1	301 766
ropinirole	insignificant	4	3	0	1	221 698
<b>benserazide</b>	insignificant	5	3	0	2	<b>C 928 981</b>
entacapone	low	5*	3	0	2*	69 289
						<b>C 254 111</b>
<b>carbidopa</b>	cannot be excl	5*	3*	0	2*	<b>C 1 183 091</b>
selegiline	cannot be excl	-	-	0	-	120 664
biperiden	cannot be excl	-	-	-	2*	225 376
rasagiline	cannot be excl	-	-	-	3*	166 376
cabergoline	cannot be excl	-	-	-	-	21 492
tolcapone	cannot be excl	-	-	-	-	3 367
trihexyphenidyl	cannot be excl	-	-	-	-	283 780
bromocriptine		9*	3	3*	3	130 929
<b>Psycholeptics</b>						
<b>lithium</b>	exempt					
<b>olanzapin</b>	insignificant	2	0	0	2	2 045 972
clomethiazole	insignificant	4	3	0	1	167 019
palperidone	insignificant	4	3	0	1	173 622
midazolam	insignificant	5	3	0	2	102 441
<b>risperidone</b>	insignificant	5	3	0	2	630 888
zolpidem	insignificant	5	3	0	2	8 930 134
<b>quetiapine</b>	insignificant	5*	3	0	2*	979 474
ariPIPrazole	insignificant	6	3	0	3	551 905
haloperidol	insignificant	8*	3*	3	2	671 436
<b>clozapine</b>	low	9	3	3	3	439 148
buspirone	cannot be excl	6*	3	0	3*	211 879
fluphenazine	cannot be excl	6*	3	0	3*	18 000
prochlorperazine	cannot be excl	8*	3	3*	2*	95
<b>zopiclone</b>	cannot be excl	8*	3	3*	2*	17 448 676
levomepromazine	cannot be excl	9*	3*	3	3	175 263
<b>propiomazine</b>	cannot be excl	9*	3*	3	3*	10 568 219
<b>hydroxyzine</b>	cannot be excl	-	-	0	-	2 427 691
sertindole	cannot be excl	-	-	0	-	698
<b>perphenazine</b>	cannot be excl	-	-	3	-	335 858
alprazolam	cannot be excl	-	-	-	-	1 660 318
chlorprothixene	cannot be excl	-	-	-	-	20 209
<b>diazepam</b>	cannot be excl	-	-	-	-	2 572 760
flupentixol	cannot be excl	-	-	-	-	168 711
lorazepam	cannot be excl	-	-	-	-	127 478
melatonin	cannot be excl	-	-	-	-	1 606 050
melperone	cannot be excl	-	-	-	-	9 242
nitrazepam	cannot be excl	-	-	-	-	1 200 655
<b>oxazepam</b>	cannot be excl	-	-	-	-	2 365 200

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
triazolam	cannot be excl	-	-	-	-	78 441
zaleplon	cannot be excl	-	-	-	-	89 964
ziprasidone	cannot be excl	-	-	-	-	83 805
<b>zuclopentixol</b>	cannot be excl	-	-	-	-	508 594
<b>Psychoanaleptics</b>						
moclobemide	insignificant	4	3	0	1	72 602
<b>venlafaxine</b>	insignificant	5	3	0	2	4 950 176
<b>methylphenidate</b>	insignificant	5	3	0	2	7 473 723
<b>mirtazapine</b>	insignificant	5	3	0	2	4 840 087
<b>rivastigmine</b>	insignificant	5	3	0	2	319 617
<b>atomoxetine</b>	insignificant	6	3	0	3	371 043
fluvoxamine	insignificant	6	3	0	3	18 916
duloxetine	low	6	3	0	3	2 489 289
<b>fluoxetine</b>	low	6	3	0	3	4 097 204
galantamine	low	6	3	0	3	1 009 031
<b>sertraline</b>	moderate	6	3	0	3	13 930 724
maprotiline	cannot be excl	6	3	0	3	12 664
trimipramine	cannot be excl	6	3	0	3	4 187
<b>amitriptyline</b>	cannot be excl	6*	3*0	3*		1 192 294
<b>citalopram</b>	cannot be excl	6*	3*0	3*		13 809 518
<b>donepezil</b>	cannot be excl	6*	3	0	3*	673 839
escitalopram	cannot be excl	6*	3*0	3*		4 821 189
paroxetine	cannot be excl	6*	3	0	3*	1 761 486
nortriptyline	cannot be excl	9*	3	3	3*	75 323
<b>memantine</b>	cannot be excl	-	-	0	-	860 549
mianserin	cannot be excl	-	-	0	-	170 768
modafinil	cannot be excl	-	-	0	-	144 121
caffeine	cannot be excl	-	-	-	-	32 689
						<b>C -</b>
reboxetine	cannot be excl	-	-	-	-	81 064
<b>clomipramine</b>		6	3	0	3	572 889
imipramine		9	3	3	3	1 025
<b>Other nervous system drugs</b>						
<b>acamprosate</b>	insignificant	3	3	0	0	196 825
nicotine	insignificant	3	0	0	3	112 369
bupropion	insignificant	6	3	0	3	823 970
buprenorphine	insignificant	6*	3	0	3*	806 130
						<b>C 210 964</b>
varenicline	insignificant	9	3	3	3	315 959
naloxone	cannot be excl	4	3	0	1	-
						<b>C 331 265</b>
pilocarpine	cannot be excl	6*	3	0	3*	882 205
						<b>C 3 357 090</b>

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
riluzole	cannot be excl	8*	3	3*	2*	33 964
methadone	cannot be excl	-	-	0	-	1 093 371
ambenonium	cannot be excl	-	-	-	-	9 472
<b>disulfiramum</b>	cannot be excl	-	-	-	-	413 100
						<b>C -</b>
neostigmine	cannot be excl	-	-	-	-	2 763
						<b>C 22 010</b>
pyridostigmine		6*	3*0	3		100 595

## P Antiparasitic Products, Insecticides and Repellents

### Antiprotozoals

mefloquine	insignificant	6	3	0	3	11 470
proguanil	insignificant	6	3	0	3	-
						<b>C 86 580</b>
lumefantrine	insignificant	8	3	3	2	<b>C 91</b>
artemether	insignificant	9	3	3	3	<b>C 91</b>
metronidazole	cannot be excl	6*	3	0	3*	203 434
						<b>E 24 545</b>
hydroxychloroquine	cannot be excl	8*	3*3	2*		120 636
atovaquone	cannot be excl	9	3	3	3	874
						<b>C 86 580</b>
pentamidine	cannot be excl	-	-	0	-	938
chloroquine	cannot be excl	-	-	-	-	23 081
phosphate						
tinidazole	cannot be excl	-	-	-	-	6 704

### Anthelmintics

mebendazole	cannot be excl	9*	3*3	3		18 348
niclosamide	cannot be excl	-	-	-	-	211
pyrvin	cannot be excl	-	-	-	-	242

### Ectoparasiticides, incl scabicides, insecticides and repellents

permethrin	moderate	9	3	3	3	-
benzyl benzoate	cannot be excl	-	-	-	-	<b>C -</b>
disulfiramum	cannot be excl	-	-	-	-	413 100

**C, E -**

## R Respiratory System

### Nasal preparations

levocabastine	insignificant	4	3	0	1	51 700
triamcinolone	insignificant	4*	3	0	1*	165 311
						<b>E -</b>

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>budesonide</b>	insignificant	5	3	0	2	8 079 288 <b>C 8 099 610</b>
<b>mometasone</b>	low	5	3	0	2	9 459 810 <b>E -</b>
sodium cromoglycate	cannot be excl	3*	3*	0	0*	103 116
oxymetazoline	cannot be excl	5*	3*	0	2*	107 342
fluticasone	cannot be excl	6	3	0	3	2 294 110 <b>C, E 2 903 190</b>
beclomethasone	cannot be excl	6*	3	0	3*	81 203 <b>C 8 099 610</b>
<b>ipratropium</b>	cannot be excl	6*	3	0	3*	736 412 <b>C 508 958</b>
xylometazoline	cannot be excl	7*	3	3	1*	13 063 <b>C 1 938</b>
azelastine	cannot be excl	-	-	-	-	3 551 <b>C -</b>
dexbrompheniramine	cannot be excl	-	-	-	-	<b>C 800</b>
phenylpropanolamine	cannot be excl	-	-	-	-	976 180 <b>C 19 900</b>
pseudoephedrine	cannot be excl	-	-	-	-	<b>C 800</b>
<b>Throat preparations</b>						
gramicidin	cannot be excl	-	-	-	-	6 269
<b>Drugs for obstructive airway diseases</b>						
<b>montelukast</b>	insignificant	2	0	0	2	2 629 921
indacaterol	insignificant	3	3	0	0	361 050
<b>terbutaline</b>	insignificant	3	3	0	0	3 851 045
bambuterol	insignificant	4	3	0	1	9 326
<b>formoterol</b>	insignificant	4	3	0	1	978 158 <b>C 8 099 610</b>
<b>budesonide</b>	insignificant	5	3	0	2	8 079 288 <b>C 8 099 610</b>
<b>salmeterol</b>	insignificant	5	3	0	2	377 580 <b>C 2 903 190</b>
mometasone	low	5	3	0	2	9 459 810 <b>E -</b>
ephedrine	cannot be excl	0*	0	0	0*	65 600 <b>C -</b>
sodium cromoglycate	cannot be excl	3*	3*	0	0*	103 116
<b>salbutamol</b>	cannot be excl	4*	3	0	1*	3 253 297 <b>C 507 020</b>
<b>tiotropium bromide</b>	cannot be excl	4*	3	0	1*	4 774 880
<b>fluticasone</b>	cannot be excl	6	3	0	3	2 294 110 <b>C, E 11 002 800</b>

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
beclomethasone	cannot be excl	6*	3	0	3*	81 203 <b>C 8 099 610</b>
<b>ciclesonide</b>	cannot be excl	6*	3	0	3*	316 080
<b>ipratropium</b>	cannot be excl	6*	3	0	3*	736 412 <b>C 508 958</b>
<b>theophylline</b>	cannot be excl	-	-	0	-	146 679
<b>Cough and cold preparations</b>						
codeine	insignificant	4	3	0	1	96 869 <b>C 6 315 472</b>
ambroxol	insignificant	5	3	0	2	278
chlorcyclizine	insignificant	5	3	0	2	<b>C 13 925</b>
bromhexine	cannot be excl	6	3	0	3	103 251 <b>C -</b>
guaifenesin	cannot be excl	-	-	0	-	262 <b>C -</b>
acetylcysteine	cannot be excl	-	-	-	-	4 624 498 <b>C -</b>
diphenhydramine	cannot be excl	-	-	-	-	<b>C -</b>
ethylmorphine	cannot be excl	-	-	-	-	<b>C -</b>
noscapine	cannot be excl	-	-	-	-	7 816 <b>C 8 600</b>
pentoxyverine	cannot be excl	-	-	-	-	-
<b>Antihistamines for systemic use</b>						
thiethylperazine	insignificant	6	3	0	3	15
fexofenadine	insignificant	6*	3	3*	0	433 165
ebastine	insignificant	8	3	3	2	892 710
loratadine	low	6	3	0	3	3 632 700
<b>desloratadine</b>	cannot be excl	5*	3	0	2*	7 136 977
<b>alimemazine</b>	cannot be excl	9*	3	3	3*	2 915 010
clemastine	cannot be excl	9*	3*	3	3	833 816
ciproheptadine	cannot be excl	9*	3	3	3*	1 110
acrivastine	cannot be excl	-	-	0	-	-
<b>cetirizine</b>	cannot be excl	-	-	0	-	3 844 354
dexchlorpheniramine	cannot be excl	-	-	-	-	-
dimenhydrinate	cannot be excl	-	-	-	-	26 466 <b>C 84</b>
<b>meclozine</b>	cannot be excl	-	-	-	-	152 585
mizolastine	cannot be excl	-	-	-	-	-

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>S Sensory Organs</b>						
<b>Ophthalmologicals</b>						
aciclovir	insignificant	4	3	0	1	95 121 <b>E -</b>
levocabastine	insignificant	4	3	0	1	51 700
dorzolamide	cannot be excl	3*	3	0	0*	257 115 <b>C 3 357 090</b>
<b>sodium cromoglycate</b>	cannot be excl	3*	3*0	0*		103 116
nedocromil	cannot be excl	3*	3*0	0*		-
<b>fusidic acid</b>	cannot be excl	6*	3	0	3*	5 493 <b>E -</b>
moxifloxacin	cannot be excl	6*	3	0	3*	13 481
pilocarpine	cannot be excl	6*	3	0	3*	882 205 <b>C 3 357 090</b>
naphazoline	cannot be excl	7*	3	3*	1*	- <b>C -</b>
antazoline	cannot be excl	8*	3	3*	2*	<b>C -</b>
ketotifen	cannot be excl	9*	3	3*	3	-
apraclonidine	cannot be excl	-	-	0	-	8 401
atropine	cannot be excl	-	-	0	-	25 068 <b>C -</b>
betaxolol	cannot be excl	-	-	0	-	84 490
brinzolamide	cannot be excl	-	-	0	-	823 150 <b>C 3 357 090</b>
carbachol	cannot be excl	-	-	0	-	-
cyclopentolate	cannot be excl	-	-	0	-	-
dexamethasone	cannot be excl	-	-	0	-	38 441 <b>C -</b>
<b>emedastine</b>	cannot be excl	-	-	0	-	-
fluorescein	cannot be excl	-	-	0	-	- <b>C -</b>
hydrocortisone	cannot be excl	-	-	0	-	401 062 <b>C, E -</b>
nepafenac	cannot be excl	-	-	0	-	-
olopatadine	cannot be excl	-	-	0	-	-
prednisolone	cannot be excl	-	-	0	-	5 381 008 <b>E -</b>
rimexolone	cannot be excl	-	-	0	-	-
<b>timolol</b>	cannot be excl	-	-	0	-	3 444 535 <b>C 3 357 090</b>
tobramycin	cannot be excl	-	-	0	-	7 113 <b>C -</b>

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
<b>V Various</b>						
<b>All other therapeutic products</b>						
deferoxamine	insignificant	1*	0	0	1*	-
flumazenil	insignificant	4	3	0	1	-
sugammadex	insignificant	4*	3	0	1*	-
deferasirox	insignificant	6	3	0	3	-
naloxone	cannot be excl	4	3	0	1	- <b>C 331 265</b>

SUBSTANCE	RISK	PBT	P	B	T	VOLUME IN DDD
fomepizole	cannot be excl	-	-	0	-	-
<b>polystyrene sulfonate</b>	cannot be excl	-	-	0	-	32 044
dexrazoxane	cannot be excl	-	-	-	-	7
<b>Diagnostic agents</b>						
hexaminlevulinate	cannot be excl	-	-	-	-	-
<b>Contrast media</b>						
gadodiamide	insignificant	3	3	0	0	-
iodixanol	insignificant	3	3	0	0	-
iohexol	insignificant	3	3	0	0	-
iomeprol	insignificant	3	3	0	0	-
iopromide	insignificant	3	3	0	0	-
gadopentetic acid	insignificant	4	3	0	1	-
gadoxetic acid	insignificant	4	3	0	1	-
gadobutrol	cannot be excl	4*	3	0	1*	-
amidotrizoic acid	cannot be excl	-	-	-	-	-
ferumoxsil	cannot be excl	-	-	-	-	-
gadoteric acid	cannot be excl	-	-	-	-	-
gadoversetamide	cannot be excl-	-	-	-	-	-
iobitridol	cannot be excl	-	-	-	-	-
ioversol	cannot be excl-	-	-	-	-	-
ioxaglic acid	cannot be excl	-	-	-	-	-
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## Reading tips

- **Pharmaceuticals in a Healthy Environment  
MistraPharma Research 2008-2011**

This book – the fourth in an annual series – takes stock of the first four years of the Swedish research programme MistraPharma. Published in 2012.  
[www.mistrapharma.se](http://www.mistrapharma.se)

- **Results from the Swedish National Screening Programme 2010. Subreport 3. Pharmaceuticals**

A screening study of 101 pharmaceuticals in wastewater, surface water and drinking water. IVL, Swedish Environmental Research Institute 2011.  
[www.ivl.se](http://www.ivl.se)

- **Environment and Pharmaceuticals**

A publication containing facts and reflections about how pharmaceutical products and pharmaceutical residues can affect our environment and, as a result, our health. Published in 2005 in collaboration between Apoteket AB, Stockholm County Council and Stockholm University.

- **Environmental Impact of Pharmaceuticals as well as Cosmetics and Hygiene Products**

The Swedish Medical Products Agency: report 2004. (Summary in English).  
[www.lakemedelsverket.se](http://www.lakemedelsverket.se)

- **Fass.se**

The Swedish Association of the Pharmaceutical Industry's website.  
[www.fass.se](http://www.fass.se)

More reading tips are available at the non-commercial website  
[www.janusinfo.se/environment](http://www.janusinfo.se/environment)

## Vocabulary

**ATC:** (Anatomic Therapeutic Chemical classification system) a classification system for drugs i.a used by WHO. The drugs are divided into 14 main groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. The same substance may have several different ATC classifications if the substance is a part of several groups and is being sold in combinations with other substances.

**Bioaccumulation:** accumulation in adipose tissue of aquatic organisms, according to the OECD based on the partition coefficient n-octanol/water, Pow, in which substances with log Pow >4 are judged to be potentially bio-accumulating (OECD test 107 or 117).

**DDD:** (Defined Daily Doses), the DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. DDD:s are not established for all preparations. In Sweden, DDD:s are also used for estimating pharmaceuticals for external use (1 gram = 1 DDD). This estimate is not based on the amount of an active substance and can therefore not be compared to the DDD for drugs for internal use.

**Environmental hazard:** the inherent environmentally damaging characteristics of the substance in the following terms: Persistence, Bio-accumulation and Toxicity (PBT).

**Environmental risk:** refers to toxic risk to the aquatic environment and is based on PEC/PNEC.

**Metabolite:** any substance produced during metabolism (digestion or other bodily chemical processes). The term metabolite may also refer to the product that remains after a drug is broken down (metabolized) by the body.

**PBT Index:** the total of the values for Persistence, Bioaccumulation and Toxicity comprises the PBT Index of the substance.

**PEC:** (Predicted Environmental Concentration), predicted environmental concentration of the substance.

**Persistence:** ability to resist degradation in the aquatic environment. The biodegradability is assessed based on criteria for readily biodegradation according to the test guidelines (test 301) of OECD or another equivalent test of biodegradability.

**PNEC:** (Predicted No Effect Concentration) the highest concentration of the substance that does not have a harmful effect on the environment.

**Toxicity:** the potential to poison aquatic organisms. Toxicity for aquatic organisms is assessed based on the results of toxicity tests including three trophic levels; fish, Daphnia and algae (OECD test guidelines 203, 202 and 201, or equivalent). Data for the most sensitive organisms are used in the assessment.

**Wise List:** (Kloka Listan) a list of recommended pharmaceuticals for common diseases in Stockholm County Council. The Wise List takes cost-effectiveness and environmental impact into account when comparing medications that are equally safe and equally suitable for the purpose, based on scientific documentation.

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## What You as a Prescriber Can Do

- Follow "Kloka Listan" (the Wise List) – environmental considerations are included. The Wise List is a list of recommended pharmaceuticals for common diseases in Stockholm County Council, issued by the Drug and Therapeutics Committee. When the Committee chooses to recommend a pharmaceutical, cost-effectiveness and environmental impact are taken into account, when comparing medications that are equally safe and equally suitable for the purpose.
- Prescribe starter packs.
- Do not prescribe more medications than can be used; if in doubt, repeating the prescription is preferable.
- Prescribe refill packs, if available.
- Ask the representatives of the pharmaceutical manufacturers about environmental impact.
- Learn more about which of “your” drugs have the largest environmental impact. If they are not recommended on the Wise List, can they be replaced by others which are?
- Tell your patients to return medical patches, vaginal rings etcetera to the pharmacy after use (especially important for those containing estrogens).

## Advice For Your Patient

- Return unused medications to the pharmacy. This is also important for used estrogen patches/vaginal rings since a lot of the estrogen remains in the patch/vaginal ring after use. Avoid flushing them down the toilet. Even inhalers can still contain active substance after being used.
- Ask for refill packs.
- Follow the enclosed instructions for using the medication carefully.
- Return empty packages to the waste recycle station.
- Use refills whenever possible.

This folder presents the environmental assessments for pharmaceutical substances. The pharmaceuticals are assessed both in terms of their inherent capacity to affect the environment (environmental hazard), and as regarding the environmental risk posed by the pharmaceutical substances when used at their current extent.

When assessing the environmental impact of a substance, consideration should be given to both environmental hazard and environmental risk, as these terms elucidate different properties of the substance.

The folder also provides concrete advice on what you can do in your daily work-life to reduce the risk of negative environmental impact from pharmaceuticals.

## For more information

More information is available at the non-commercial website Janusinfo, produced by the Stockholm County Council:  
[www.janusinfo.se/environment](http://www.janusinfo.se/environment)

This information is continuously updated.

## You can also contact

Janusinfo's editorial office for questions about the PBT Index and the Wise List:  
e-mail: [janusredaktionen@sll.se](mailto:janusredaktionen@sll.se)



The Council has to carry out its mandate in a way which is climate efficient and resource efficient as well as conducting health-promotive environmental work. This includes reducing the environmental risk from pharmaceuticals and lowering the levels of the most environmentally straining pharmaceutical substances in the environment.



Tryckt hos Åtta.45 AB, 2013