FASS

Imigran®

GlaxoSmithKline

Nässpray, lösning 20 mg
(klar ljusgul till mörkgul vätska)

Medel mot migrän

Aktiv substans:
Sumatriptan

ATC-kod:
N02CC01

Läkemedel från GlaxoSmithKline omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Sumatriptan

Miljörisk: Användning av sumatriptan har bedömts medföra försumbar risk för miljöpåverkan.
Nedbrytning: Sumatriptan är potentiellt persistent.
Bioackumulering: Sumatriptan har låg potential att bioackumuleras.

Detaljerad miljöinformation

Detailed background information
Environmental Risk Classification
Predicted Environmental Concentration (PEC)
PEC is calculated according to the following formula:
PEC (µg/L) = $(A*10^{9}*(100-R))/(365*P*V*D*100) = 1.37*10^{-6}*A(100-R)$

PEC = 0.062 µg/L

Where:
A = 454.22 kg (total sold amount of API free base in Sweden year 2022, data from IQVIA). Total volume of Sumatriptan succinate = 635.08 = 450.91 Sumatriptan free base. Total Sumatriptan = 450.91 + 3.31 = 454.22.

R = 0% removal rate (conservatively, it has been assumed there is no loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation)
P = number of inhabitants in Sweden = $10 * 10^6$
V (L/day) = volume of wastewater per capita and day = 200 (ECHA default) (Ref. I)
D = factor for dilution of waste water by surface water flow = 10 (ECHA default) (Reference 1)

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

Green Algae (Scenedesmus subspicatus):
IC50 96h (growth) = 26,000 µg/L (OECD 201) (Reference 5)
NOEC = 12,500 µg/L

Water flea (Daphnia pulex):
Acute toxicity
EC50 96h (immobility) = 290,000 µg/L (OECD 202) (Reference 9)

Water flea (Ceriodaphnia dubia):
Chronic toxicity
NOEC 8 days (reproduction) = 23,000 µg/L (USEPA 1002) (Reference 8)

Rainbow Trout (Salmo gairdneri):
Acute toxicity
LC50 96 h (lethality) > 71,000 µg/L (OECD 203) (Reference 6)

Fish:
Chronic toxicity
No data

Other ecotoxicity data:
Microorganisms in activated sludge:
EC50 3 h (inhibition) > 750,000 µg/L @ 3 hrs (OECD 209) (Reference 11)
NOEC = 100 000 µg/L

PNEC = 12,500/50 = 250 µg/L

PNEC (µg/L) = lowest NOEC/10, where 50 is the assessment factor applied for two long-term NOECs. NOEC for alga (= 12,500 ug/L) has been used for this calculation since it is the most sensitive of the three tested species.

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.062/250= 2.49×10^{-4}, i.e. PEC/PNEC ≤ 0.1 which justifies the phrase “Use of sumatriptan has been considered to result in insignificant environmental risk.”

Degradation

Biotic degradation

Ready degradability:
1% degradation in 28 days (OECD 301). (Reference 9)

Inherent degradability:

17% ultimate (DOC) degradation in 28 days (OECD 302B). (Reference 7)
100% primary (parent) degradation in 16 days
This may be regarded as evidence for inherent primary biodegradation. This substance is not inherently biodegradable.
Aerobic Degradation in Soil
32.1% - 40.2% degradation in 64 days (TAD 3.12) (Reference 4)

Abiotic degradation

Hydrolysis:
No data

Photolysis:
No data

Justification of chosen degradation phrase:
Sumatriptan is not readily degradable nor inherently biodegradable. This substance will be subject to moderate degradation in soil matrices. However, the relevant degradation products have not been identified or characterised. The phrase “Sumatriptan is potentially persistent” is thus chosen.

Bioaccumulation

Partitioning coefficient:
Log Dow = -2.3 at pH 7 (TAD 3.02). (Reference 3)

Log Dow at pH 5 = -2.0
Log Dow at pH 7 = -2.3
Log Dow at pH 9 = -0.5

Justification of chosen bioaccumulation phrase:
Since log Dow < 4 at pH 7, the substance has low potential for bioaccumulation.

Excretion (metabolism)

Following oral administration, sumatriptan is rapidly absorbed, 70% of maximum concentration occurring at 45 minutes. After 100mg dose, the maximum plasma concentration is 54ng/ml. Mean absolute oral bioavailability is 14% partly due to presystemic metabolism and partly due to incomplete absorption. The elimination phase half-life is approximately 2 hours, although there is an indication of a longer terminal phase. Plasma protein binding is low (14-21%), mean volume of distribution is 170 litres. Mean total plasma clearance is approximately 1160ml/min and the mean renal plasma clearance is approximately 260ml/min. Non-renal clearance accounts for about 80% of the total clearance. Sumatriptan is eliminated primarily by oxidative metabolism mediated by monoamine oxidase A. The major metabolite, the indole acetic acid analogue of Sumatriptan is mainly excreted in the urine, where it is present as a free acid and the glucuronide conjugate (Reference 2).

Please, also see Safety data sheets on http://www.msds-gsk.com/ExtMSDSlist.asp.

References

1. ECHA, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment.
2. Pharmacokinetic properties: Meatbolism and Elimination. Summary of Product Characteristics Imigran (Sumatriptan succinate) Tablets. GlaxoSmithKline, July 2013.

3. Cowlyn TC. GR43175X: Determination of Physico-Chemical Properties. Report No. 94/GLX169/1033. Pharmaco LSR, February 1995.
4. Morgan P. GR43175X: Biodegradation in Soil. Report No. 94/GLX170/0782. Pharmaco LSR, February 1995.
5. Vryhenhoef J and McKenzie J. Sumatriptan succinate: Algal Inhibition Test. Report No. 1127/543. Safepharm Laboratories Limited, July 2004.
6. Wetton PM and McKenzie J. Sumatriptan succinate: Acute Toxicity to Rainbow Trout (Oncoryhynchus mykiss). Report No. 1127/542. Safepharm Laboratories Limited, July 2004.
7. Clarke N and McKenzie J. Sumatriptan succinate: Assessment of Inherent Biodegradability; Modified Zahn-Wellens/EMPA Test. Report No. 1127/544. Safepharm Laboratories Limited, August 2004.
8. Wetton PM. Sumatriptan succinate: Daphnid: Ceriodaphnia Dubia Survival and Reproduction Test. Report No. 1127/0953. Safepharm Laboratories Limited, March 2006.
9. Material Safety Data Sheet for Imitrex Tablets. SDS number 110562. GlaxoSmithKline plc, October 2013.