FASS

Lamictal®

GlaxoSmithKline

Tuggtablett/dispergerbar tablett 2 mg
(Vit till gulvit och kan vara lätt marmorerad. Den luktar svartvinbär. Tabletten är 4,8 mm lång, rund och märkt "LTG" ovanför siffran "2" på ena sidan och med två överlappande ovaler i rät vinkel på den andra sidan.)

Antiepileptikum

Aktiv substans:
Lamotrigin

ATC-kod:
N03AX09

Läkemedel från GlaxoSmithKline omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Lamotrigin

Miljörisk: Användning av lamotrigin har bedömts medföra försumbar risk för miljöpåverkan.
Nedbrytning: Lamotrigin är potentiellt persistent.
Bioackumulering: Lamotrigin 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) = $(A*10^{9}*(100-R))/(365*P*V*D*100) = 1.5*10^{-6}$ *A(100-R)

PEC = 0.47 µg/L

Where:
A = 3,150.23 kg (total sold amount API in Sweden year 2015, data from IMS Health). Reduction of A may be justified based on metabolism data.

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 = $9 *10^{6}$

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) (Ref. I)

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

Green Algae (Scenedesmus subspicatus):
IC50 96h (growth) = 39,700 µg/L (OECD 201) (Reference 7)
NOEC = 7,500 µg/L

Water flea (Daphnia magna):
Acute toxicity
EC50 48 h (immobility) = 56,000 µg/L (OECD 202) (Reference 8)

Water flea (Ceriodaphnia dubia):
Chronic toxicity
NOEC 8 days (reproduction) = 10,000 µg/L (USEPA 1002) (Reference 10)

Rainbow Trout (Oncorhyncus mykiss):
Acute toxicity
LC50 96 h (lethality) = 85,000 µg/L (OECD 203) (Reference 9)

Fish:
Chronic toxicity
No data

Other ecotoxicity data:
Microorganisms in activated sludge:
EC50 3 h (inhibition) = 1,000,000 µg/L @ 3 hrs (OECD 209) (Reference 5)

PNEC = 7,500/50 = 150 µg/L
PNEC (µg/L) = lowest NOEC/50, where 50 is the assessment factor applied for two long-term NOECs. NOEC for alga (= 7 500 µg/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 = 0.47/150= 0.0031, i.e. PEC/PNEC ≤ 0.1 which justifies the phrase “Use of lamotrigine has been considered to result in insignificant environmental risk.”

Degradation

Biotic degradation

Ready degradability:

<1% degradation in 28 days (TAD 3.11). (Reference 4)

Inherent degradability:

<10% degradation in 28 days (OECD 302). (Reference 6)

Abiotic degradation

Hydrolysis:

No data

Photolysis:

No data

Justification of chosen degradation phrase:

Lamotrigine is not readily degradable or inherently degradable. The phrase “Lamotrigine is potentially persistent” is thus chosen.

Bioaccumulation

Partitioning coefficient:

Log Dow = 1.54 at pH 7.4 (TAD 3.02). (Reference 3)

Log Dow at pH 5 < 1

Log Dow at pH 7 = 1.4
Log Dow at pH 9 = 1.4

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

Excretion (metabolism)

UDP-glucuronyl transferases have been identified as the enzymes responsible for metabolism of lamotrigine. Lamotrigine induces its own metabolism to a modest extent depending on dose. However, there is no evidence that lamotrigine affects the pharmacokinetics of other AEDs and data suggest that interactions between lamotrigine and medicinal products metabolised by cytochrome P450 enzymes are unlikely to occur.

The apparent plasma clearance in healthy subjects is approximately 30 mL/min. Clearance of lamotrigine is primarily metabolic with subsequent elimination of glucuronide-conjugated material in urine. Less than 10% is excreted unchanged in the urine. Only about 2% of lamotrigine-related material is excreted in faeces (Reference 2).

PBT/vPvB assessment

Lamotrigine does not fulfil the criteria for PBT and/or vBvP.

All three properties, i.e. ‘P’, ‘B’ and ‘T’ are required in order to classify a compound as PBT (Reference 1). Lamotrigine does not fulfil the criteria for PBT and/or vBvP based on log Pow < 4.

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.
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3. Lamictal Environmental Information Document. Report No. GCPV/91/0005-01. Burroughs Wellcome Co., January 1993.
4. Blasberg J. Aerobic Biodegradation in Water Using 14-C-Lamotrigine. Report No. 40510. ABC Laboratories, November 1992.
5. Lamotrigine: Activated Slude, Respiration Inhibiton Test. Test No. 91-04-232-01. AATCC Testing Services, April 1991.
6. Stewart KM, Smyth DV, Kent SJ. Lamotrigine: Determination of Inherent Biodegradability (Zahn-Wellens test). Report No. BL7683/B. Brixham Environmental Laboratory, October 2004.
7. Kent SJ and Swarbrick RH. Lamortrigine: Toxicity to the green alga Selenastrum capricornutum. Report No. BL7681/B. Brixham Environmental Laboratory, August 2004.
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9. Kent SJ and Swarbrick RH. Lamortrigine: Acute Toxicity to rainbow trout (Oncoryhynchus mykiss). Report No. BL7682/B. Brixham Environmental Laboratory, August 2004.

10. Young BE and Kent SJ. Lamortrigine: Determination of the 3 brood (7 day) chronic toxicity to Ceriodaphnia dubia. Report No. BL8147/B. Brixham Environmental Laboratory, March 2006.