FASS

Tegretol Retard (Parallellimporterat)

M

Cross Pharma AB

Depottablett 200 mg

Avregistreringsdatum: 2007-06-30 (Tillhandahålls ej)

Inga avvikelser.

Antiepileptikum

Visa information om det parallellimporterade läkemedlet

Aktiv substans:

Karbamazepin

ATC-kod:

N03AF01

För information om det avregistrerade läkemedlet omfattas av Läkemedelsförsäkringen, kontakta Läkemedelsförsäkringen.

Läs mer om avregistrerade läkemedel

Miljöpåverkan

Miljöinformationen för karbamazepin är framtagen av företaget Novartis för Tegretol®, Tegretol® Retard

Miljörisk: Användning av karbamazepin har bedömts medföra låg risk för miljöpåverkan.

Nedbrytning: Karbamazepin är potentiellt persistent.

Bioackumulering: Karbamazepin har låg potential att bioackumuleras.

Detaljerad miljöinformation

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

PEC (µg/L) = $(A*10^{9}*(100-R))/(365*P*V*D*100) = 1.5*10^{-6} * A * (100 – R) = 1.5*10^{-6} * 5804.9704$ kg * 100

PEC = 0.871 µg/L

Where:

A = 5804.9704 kg (total sold amount API in Sweden year 2015, data from IMS Health).

R = 0 % removal rate (due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation) = 0 if no data is available.

P = number of inhabitants in Sweden = $9 *10^{6}$

V (L/day) = volume of wastewater per capita and day = 200 (ECHA default) (ECHA 2008)

D = factor for dilution of waste water by surface water flow = 10 (ECHA default) (ECHA 2008)

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

Algae (Pseudokirchneriella subcapitata) (method unknown) (Harada et al. 2008)*:*

NOEC = 0.5 mg/L

Crustacean:
Acute toxicity *(Daphnia magna)*
EC50 48 h (immobilisation) > 100.0 mg/L (OECD202) (Ciba-Geigy Crop Protection AG Project No.: 880059)
Chronic toxicity (*Cerodaphnia dubia)*
NOEC 7 days (reproduction) = 0.025 mg/L (AFNOR T90-376, 2000) (Ferrari et al. 2003)

Fish:
Acute toxicity (*Danio rerio,* zebra fish)
LC50 96 h (mortality) = 43.0 mg/L (OECD203) (Ciba-Geigy Crop Protection AG Project No.: 870093)
Chronic toxicity (*Danio rerio*, zebra fish)
NOEC 10 days (mortality) = 25.0 mg/L (Early life-stage toxicity study, ISO 12890) (Ferrari et al., 2003)

Other ecotoxicity data:
Bacterial respiration inhibition
EC_{50} 3h > 320.0 mg/L (activated sludge respiration inhibition) (OECD209) (Ciba-Geigy Project No.: 0048466)

Sediment-dwelling organisms (*Chironomus riparius*, non-biting midge)
NOEC 28 days (inhibition of emergence) = 0.625 mg/L (OECD 218) (Nentwig et al. 2004)

PNEC derivation:
PNEC = 2.5 µg/L
PNEC (µg/L) = lowest NOEC/10, where 10 is the assessment factor used if three chronic toxicity studies from three trophic levels are

available. The NOEC for *Cerodaphnia dubia* reproduction has been used to derive the PNEC for carbamazepine.

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.871 µg/L / 2.5 µg/L = 0.3484, i.e. PEC/PNEC ≤ 1 which justifies the phrase "Use of carbamazepine has been considered to result in low environmental risk."

Degradation

Biotic degradation

Ready degradability:

0 % degradation in 28 days, not readily biodegradable (OECD 301E). (Ciba-Geigy, Ecotoxicology, Project No.: 811770)

Simulation studies:

DT_{50} (total system) = 328 days (OECD 308). (Löffler et al. 2005)

Justification of chosen degradation phrase:

Based on the fact that carbamazepine is not readily biodegradable and according to the pass criteria for OECD308 studies, carbamazepine can be classified as ‘Carbamazepine is potentially persistent.’

(DT50 for total system > 120 days)

Bioaccumulation

Partitioning coefficient:

Log K_{ow} = 1.51 – 1.58 (OECD107) (Scheytt et al. 2005 and Mersmann, 2003)

Justification of chosen bioaccumulation phrase:

Since log K_{ow} < 4, carbamazepine has low potential for bioaccumulation.

Excretion (metabolism)

After administration of a single oral dose of 400 mg carbamazepine, 72% is excreted in the urine and 28% in the faeces. In the urine, about 2% of the dose is recovered as unchanged drug and about 1% as the pharmacologically active 10,11-epoxide metabolite. (Novartis Core Data Sheet TEGRETOL® (carbamazepine))

PBT/vPvB assessment

Based on screening criteria, carbamazepine has low potential for bioaccumulation and can therefore not be considered a potential PBT or vPvB substance.

References

- ECHA 2008, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment. http://guidance.echa.europa.eu/docs/guidance_document/informa
- Harada A. et al, 2008, Biological effects of PPCPs on aquatic lives and evaluation of river waters. Water Science&Technology 58: 1541-1546
- Ciba-Geigy Crop Protection AG Project No.: 880059. (Full report and thus title and date not available anymore).
- Ferrari B. et al, 2003. Ecotoxicological impact of pharmaceuticals found in treated wastewaters: study of carbamazepine, clofibric acid, and diclofenac. Ecotoxicology and Environmental Safety 55: 359–370

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- Nentwig et al 2004. Effects of pharmaceuticals on the aquatic invertebrates- the example of carbamazepine and clofibric acid.
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- Löffler et al 2005. Environmental fateof pharmaceuticals in water/Sediment systems. Environmental Science & Technology 39: 5209-5218.
- Scheytt T. et al. 2005.
- Mersmann P. 2003. Transport- and Sorptionsverhalten der Arzneimittelwirkstoffe Carbamazepin, Clofibrinsäure, Diclofenac, Ibuprofen und Propyphenazon in der wassergesättigten und -ungesättigten Zone,. PhD-thesis, Technical University Berlin
- Novartis Core Data Sheet TEGRETOL® (carbamazepine). Version 1.0. 21 March 2013.