FASS

Lamivudine/Zidovudine Accord

M

Accord Healthcare AB

Filmdragerad tablett 150 mg/300 mg

Avregistreringsdatum: 2020-12-31 (Tillhandahålls ej) (vita till benvita, kapselformade, bikonvexa, filmdragerade tabletter, ca 17,5 mm lång och ca 8,0 mm bred, präglade med 'H' på ena sidan och med 'L' samt '9' på var sin sida om skåran på andra sidan)

Virushämmande medel mot hivinfektioner, kombinationer

Aktiva substanser (i bokstavsordning):

Lamivudin

Zidovudin

ATC-kod:

J05AR01

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

Läs mer om avregistrerade läkemedel

Miljöpåverkan

Miljöinformationen för lamivudin är framtagen av företaget GlaxoSmithKline för Combivir®, DOVATO, Epivir®, Kivexa, TRIZIVIR, Triumeq, Zeffix, Zeffix®

Miljörisk: Användning av lamivudin har bedömts medföra försumbar risk för miljöpåverkan.
Nedbrytning: Lamivudin bryts ned i miljön.
Bioackumulering: Lamivudin 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) = $(A*10^{9}*(100-R)/(365*P*V*D*100) = 1.37*10^{-6}$ *A(100-R)

PEC = 0.028 µg/L

Where:
A = 205.36 kg (total sold amount API in Sweden year 2020, data from IQVIA).
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) (Reference 1)
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 (Selenastrum caprocornutum):

IC50 72h (growth) > 96,900 µg/L (OECD 201) (Reference 7)
NOEC > 96,900 µg/L

Water flea (Daphnia magna):
Acute toxicity
EC50 48 h (immobility) > 1,000,000 µg/L (OECD 202) (Reference 5)
NOEC > 1,000,000 µg/L

Water flea (Ceriodaphnia dubia):
Chronic toxicity
EC50 7 days (reproduction) > 100,000 µg/L (EPA 1002) (Reference 10)
NOEC = 100,000 µg/L

Water flea (Daphnia magna):
Chronic toxicity
EC50 21 days (reproduction) > 100,000 µg/L (OECD 211) (Reference 12)
NOEC = 100,000 µg/L

Rainbow Trout (Juvenilee Oncorhyncus mykiss):
Acute toxicity
LC50 96 h (lethality) > 97,700 µg/L (OECD 203) (Reference 8)
NOEC = 97,700 µg/L

Fathead Minnow (Pimephales promelas):
Chronic toxicity
LC50 96 h (lethality) > 10,000 µg/L (OECD 210) (Reference 13)
NOEC = 10,000 µg/L

Other ecotoxicity data:

Microorganisms in activated sludge
EC50 3 hours (Inhibition) > 1,000,000 µg/L (OECD 209) (Reference 11)
NOEC = 1,000,000 µg/L

Chironomid (Chironomus riparius)
NOEC 28 days (development) = 100,000 µg/kg (OECD 218) (Reference 14)

PNEC = 10,000/10 = 1,000 µg/L

PNEC (µg/L) = lowest NOEC/10, where 10 is the assessment factor applied for three long-term NOECs. NOEC for fish (= 10,000 ug/L) has been used for this calculation since it represents the lowest value for all three tested species.

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.028/1,000 = 2.80 x 10^{-5}, i.e. PEC/PNEC ≤ 1 which justifies the phrase “Use of lamivudine has been considered to result in insignificant environmental risk.”

Degradation

Biotic degradation

Ready degradability:
< 1% degradation in 28 days (OECD 301B) (Reference 4)

Inherent degradability:
0% degradation in 28 days (OECD 302B) (Reference 9)
4% primary (loss of parent) degradation in 28 days

15-24% degradion in soil (TAD 3.12) (Reference 3)

Simulation studies:

Water-sediment study:

50% (DT_{50}) decline (total system) = 22-29 days (OECD 308)

(Reference 14)

Total Lamivudine (day 100) = 0.4% - 0.6%

CO_2 = 8.50% - 12.60%

Total Non-extractable residue = (day 100) = 18.60% - 19.10%

Extraction methods: The non-extractable radioactivity in the samples taken at 100 days was characterised using an acid/base fractionation procedure. Sediment debris was extracted with 0.5 M sodium hydroxide by shaking on an orbital shaker overnight at ambient temperature. The debris was separated by centrifugation and the supernatant removed. The debris was washed with 0.5 M sodium hydroxide and allowed to air-dry. The supernatant was adjusted to pH 1 with concentrated hydrochloric acid and left to stand at ambient temperature. The sample was centrifuged, the precipitate washed with 1 M HCl and the supernatant combined with these washings. The volume of this solution, the fulvic acid fraction, was measured and duplicate aliquots taken for radio-assay. The precipitate, the humic acid fraction, was dissolved in 0.5 M sodium hydroxide.

Abiotic degradation

Hydrolysis:

Half-life, pH 7 > 1 year (OECD 111) (Reference 4)

Photolysis:

No data

Justification of chosen degradation phrase:
Lamivudine is not readily biodegradable nor inherently biodegradable.
Lamivudine DT50 < 32 days and the presence of the parent is < 15%.
The phrase “Lamivudine is degraded in the environment” is thus chosen.

Bioaccumulation

Partitioning coefficient:
Log Dow = -1.44 at pH7. (TAD 3.02) (Reference 3)

Log Dow at pH5 = -1.17
Log Dow at pH7 = -1.44
Log Dow at pH9 = -1.86

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

Excretion (metabolism)

Lamivudine is predominately cleared unchanged by renal excretion. The likelihood of metabolic interactions of lamivudine with other medicinal products is low due to the small extent of hepatic metabolism (5-10%) and low plasma protein binding. (Reference 2)

PBT/vPvB assessment

Lamivudine 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). Lamivudine does not fulfil the criteria for PBT and/or vBvP based on a log Dow < 4.

Please, also see Safety data sheets on

http://www.msds-gsk.com/ExtMSDSlist.asp.

References

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