

**Epivir®**

M R F

**GlaxoSmithKline**

Oral lösning 10 mg/ml

(klar, färglös till svagt gul lösning, jordgubbs- och banansmak)

Antiviralt medel

**Aktiv substans:**

Lamivudin

**ATC-kod:**

J05AF05

Läkemedel från GlaxoSmithKline omfattas av  
Läkemedelsförsäkringen.

## Miljöpåverkan

### Lamivudin

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:

$$\text{PEC } (\mu\text{g/L}) = (A \cdot 10^9 \cdot (100 - R)) / (365 \cdot P \cdot V \cdot D \cdot 100) = 1.37 \cdot 10^{-6} \cdot A(100 - R)$$

$$\text{PEC} = 0.028 \mu\text{g/L}$$

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 =  $10 \cdot 10^6$

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 capricornutum):*

IC50 72h (growth) > 96,900  $\mu\text{g/L}$  (OECD 201) (Reference 7)

NOEC > 96,900  $\mu\text{g/L}$

*Water flea (Daphnia magna):*

Acute toxicity

EC50 48 h (immobility) > 1,000,000  $\mu\text{g/L}$  (OECD 202) (Reference 5)

NOEC > 1,000,000  $\mu\text{g/L}$

*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 (Juvenile Oncorhynchus 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)

$$\text{PNEC} = 10,000/10 = 1,000 \text{ µg/L}$$

*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)**

$\text{PEC/PNEC} = 0.028/1,000 = 2.80 \times 10^{-5}$ , i.e.  $\text{PEC/PNEC} \leq 1$  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% degradation in soil (TAD 3.12) (Reference 3)

#### ***Simulation studies:***

*Water-sediment study:*

50% ( $\text{DT}_{50}$ ) decline (total system) = 22-29 days (OECD 308)

(Reference 14)

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

$\text{CO}_2 = 8.50\% - 12.60\%$

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  $\log \text{Dow} < 4$ , 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  $\log \text{Dow} < 4$ .

**Please, also see Safety data sheets on**

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

## References

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- 15.** Grist A. Lamivudine: Aerobic Transformation in Aquatic Sediment Systems. Report No. TMR0048. Harlan Laboratories Limited, February 2017.