FASS

GILENYA®

Novartis

Kapsel, hård 0,5 mg
(16 mm kapsel med klargul, ogenomskinlig överdel och vit, ogenomskinlig underdel; märkt med "FTY0.5 mg" tryckt med svart färg på överdelen och med två ränder tryckta radiellt med gul färg på underdelen.)

Selektiva immunsuppressiva medel

Aktiv substans:
Fingolimod

ATC-kod:
L04AE01

Läkemedel från Novartis omfattas av Läkemedelsförsäkringen.
Läkemedlet distribueras också av företag som inte omfattas av Läkemedelsförsäkringen, se Förpackningar.

Miljöpåverkan

Fingolimod

Miljörisk: Användning av fingolimod har bedömts medföra försumbar risk för miljöpåverkan.
Nedbrytning: Fingolimod bryts ned i miljön.
Bioackumulering: Fingolimod 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 = 0.0000189 µg/L = 0.0189 ng/L

Where:
A = 0.1378 kg fingolimod hydrochloride (total sold amount API in Sweden year 2021, data from IQVIA).
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 = $10 * 10^6$
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 (Selenastrum capricornutum) (OECD 201) (NOTOX Project 305101)*:*
EC_{10} 72 h (growth rate) = 41.9 µg/L
NOEC 72 h (growth rate) = 20.3 µg/L

*Crustacean (*Waterflea, *Daphnia magna):*
Acute toxicity
EC50 48 h (immobilisation) = 120.0 µg/L (OECD202) (NOTOX Project 305112)
Chronic toxicity
NOEC 21 days (mortality of parent daphnids) = 89.0 µg/L (OECD 211) (RCC Study B54000)

*Fish (*Zebrafish, *Danio rerio):*
Chronic toxicity
NOEC 34 days (survival of larvae and juvenile fish) = 90.0 µg/L (OECD 210) (RCC Study B54022)

Other ecotoxicity data:
Bacterial respiration inhibition (activated sludge microorganisms)
EC_{10} 3 h = 20.0 mg/L (OECD209), (NOTOX Project 305123)
PNEC = 20.3 µg/L / 10 = 2.03 µg/L = 2030 ng/L
PNEC (µg/L) = lowest NOEC/10, where 10 is the assessment factor used, if chronic toxicity values for 3 trophic levels are available. NOEC from green algae growth inhibition (OECD 201) 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 = 0.0189 ng/L / 2030.0 ng/L = 9.2×10^{-6}, i.e. PEC/PNEC ≤ 0.1 which justifies the phrase "Use of fingolimod has been considered to result in insignificant environmental risk."

Degradation

Biotic degradation

Ready degradability:
0 % degradation in 28 days, not readily biodegradable (OECD301 B). (NOTOX Project 305134)

Transformation in water-sediment systems:
DT50 in total system = 0.35 – 0.39 days (OECD 308). (Harlan Laboratories Study B53998)

Study duration: 28 days
The DT50 given above refers to the loss of initially applied parent substance (initially applied radioactivity) due to its transformation, mineralization and/or irreversible binding to sediments. At the end of the study (day 28) only 0.7-0.8 % of applied radioactivity remained in the total system as parent API. Sediments were

submitted to up to three extraction steps using acetonitrile/water (4:1; v/v) at room temperature. From day 1 onwards, Soxhlet extraction using acetonitrile/water (4:1; v/v) for 4 hours was additionally performed on the extracted sediments.

Justification of chosen degradation phrase:
According to the classification scheme proposed for the OECD308 studies in the update of the 'Environmental classification of pharmaceuticals at www.fass.se - Guidance for pharmaceutical companies' of 2012, fingolimod can be classified as ‘Fingolimod is degraded in the environment'.

Bioaccumulation

Partitioning coefficient:
Log D = 3.4 (pH 7.4; dual-phase potentiometric titration) (RD-2010-00593)
Justification of chosen bioaccumulation phrase:
Since logD at pH 7.4 < 4, fingolimod has low potential for bioaccumulation.

Excretion (metabolism)

After oral administration, about 81% of the dose is slowly excreted in the urine as inactive metabolites. Fingolimod and fingolimod-phosphate are not excreted intact in urine but are the major components in the feces with amounts representing less than 2.5% of the dose each. After 34 days, the recovery of the administered dose is 89%. (Novartis Core Data Sheet, GILENYA® (fingolimod))

References

- ECHA 2008, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment. http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm
- NOTOX Project 305101: Fresh water algal growth inhibition test with FTY720/DS. Final report: 28 February 2001.
- NOTOX Project 305112: Acute toxicity study in *Daphnia magna* with FTY720/DS (static). Final report: 28 February 2001.
- RCC Study B54000: FTY720 DS: Effect on survival and reproduction of *Daphnia magna* in a semi-static test over three weeks. Final report: 09 July 2008.
- RCC Study B54022: FTY720 DS: Toxic effects to zebra fish (*Brachydanio rerio*) in an early-life stage toxicity test. Final report: 08 September 2008.
- NOTOX Project 305123: Activated sludge respiration inhibition test with FTY720/DS (contact time: 3 hours). Final report: 20 November 2000.
- NOTOX Project 305134: Determination of ‘ready’ biodegradability: carbon dioxide (CO2) evolution test (modified Sturm test) with FTY720/DS. Final report: 18 December 2000.
- RD-2010-00593: Faller B, Rodde S, Domange N. FTY720: Lipophilicity profile. Novartis Pharma AG Basel, Switzerland. Research Study report no RD-2010-00593; 02 July 2010.
- Harlan Laboratories Study B53976: 14C-FTY720 DS: Adsorption/desorption. Final report: 23 January 2009.
- Harlan Laboratories Study B53998: 14C-FTY720 DS: Route and rate of degradation in aerobic aquatic sediment systems. Final report: 20 January 2009.
- Novartis Core Data Sheet for GILENYA®(fingolimod), Version 3.4, 21 January 2019