

Tobrex Depot

M**Novartis**

Ögondroppar, lösning 3 mg/ml

Avregistreringsdatum: 2022-10-27 (Tillhandahålls ej) (Färglös lösning)

Bredspektrumantibiotikum med depoteffekt

Aktiv substans:

Tobramycin

ATC-kod:

S01AA12

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

Läs mer om avregistrerade läkemedel

Miljöpåverkan

Tobramycin

Miljörisk: Användning av tobramycin har bedömts medföra försumbar risk för miljöpåverkan.

Nedbrytning: Tobramycin är potentiellt persistent.

Bioackumulering: Tobramycin har låg potential att bioackumuleras.

Detaljerad miljöinformation

Detailed background information

PEC is calculated according to the following formula:

$$\begin{aligned} \text{PEC } (\mu\text{g/L}) &= (A \cdot 10^9 \cdot (100 - R)) / (365 \cdot P \cdot V \cdot D \cdot 100) = 1.37 \cdot 10^{-6} \cdot A \cdot \\ (100 - R) &= 1.37 \cdot 10^{-6} \cdot 10.537 \cdot 100 \\ \text{PEC} &= 0.00144 \mu\text{g/L} \end{aligned}$$

Where:

A = 10.537 kg (5.758 kg tobramycin and 5.782 tobramycinsulfat equaling 4.779 tobramycin free base) (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 = $10 \cdot 10^6$

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

Cyanobacteria / blue-green algae (Anabeana flos-aquae) (OECD 201) (NOTOX Project 488773):

EC50 72 h (growth rate) = 0.349 mg/L

NOEC = 0.051 mg/L

Crustacean (Daphnia magna, waterflea):

Chronic toxicity

NOEC 21 days (parental mortality) = 0.36 mg/L (OECD 211)
(NOTOX Project 488772)

*Fish (Fathead minnow, *Pimephales promelas*):*

Chronic toxicity

NOEC 33 days = 10 mg/L, no effect up to regulatory limit
concentration (OECD 210) (NOTOX Project 488774)

Other ecotoxicity data:

Bacterial respiration inhibition

EC₅₀ 3 h > 1000 mg/L (OECD209) (NOTOX Project 488774)

PNEC derivation:

PNEC = 5.1 µg/L

PNEC = lowest NOEC/10, where 10 is the assessment factor used if chronic toxicity data for three trophic levels is available. The NOEC for cyanobacteria 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 = 0.00144 µg/L / 5.1 µg/L = 0.000282, i.e. PEC/PNEC ≤ 0.1 which justifies the phrase "Use of tobramycin has been considered to result in insignificant environmental risk."

Degradation

Biotic degradation

Ready degradability:

0 % degradation in 28 days, not readily biodegradable (OECD 301B). (NOTOX Project 488776)

Justification of chosen degradation phrase:

Tobramycin does not fulfil the criteria for ready degradability. The phrase "Tobramycin is potentially persistent" is thus chosen.

Bioaccumulation

Partitioning coefficient:

Log P = -5.8 (method unknown). (Clarke's 2017)

Justification of the chosen bioaccumulation phrase:

Since the partitioning coefficient remains significantly below the trigger level for bioaccumulation potential, i.e. $\log K_{ow} < 4.0$, the following phrase is chosen: 'Tobramycin has low potential for bioaccumulation'.

Excretion (metabolism)

Tobramycin is not metabolized and is primarily excreted unchanged in the urine. (Novartis Core Data Sheet for TOBI[®], 2017)

References

- ECHA 2008, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment. http://guidance.echa.europa.eu/docs/guidance_document/informa
- NOTOX Project 488773. Fresh water cyanobacteria growth inhibition test with TBM100 DS. Final report: 08 April 2009.
- NOTOX Project 488772. *Daphnia magna*, reproduction test with TBM100 DS (semi-static). Final report: 12 May 2009.
- NOTOX Project 488775. Fish early-life stage toxicity test with TBM100 DS (semi-static). Final report: 12 May 2009.
- NOTOX Project 488774. Activated sludge respiration inhibition test with TBM100 DS. 4 December 2008.

- NOTOX Project 488776. Determination of 'ready' biodegradability: carbon dioxide (CO₂) evolution test (modified Sturm test) of TBM100 DS. Final report: 20 January 2009.
- Clarke's Analysis of Drugs and Poisons, Monograph on Tobramycin. Accessed: 02. March 2017.
<https://www.medicinescomplete.com/mc/clarke/current/>

Novartis Core Data Sheet for TOBI[®] (tobramycin). Version 2.1. 19 January 2017