FASS

Tobrasone

Novartis

Ögondroppar, suspension 3 mg/ml / 1 mg/ml
(Vit till benvit suspension)

Glukokortikoid i kombination med bredspektrumantibiotikum

Aktiva substanser (i bokstavsordning):
Dexametason
Tobramycin

ATC-kod:
S01CA01

Läkemedel från Novartis omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Dexametason

Miljörisk: Risk för miljöpåverkan av dexametason kan inte uteslutas då det inte finns tillräckliga ekotoxikologiska data.
Nedbrytning: Dexametason är potentiellt persistent.
Bioackumulering: Dexametason 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) = $1.37*10^{-6}$ * 6.68 kg * 100 = 0.00091 µg/L = 0.91 ng/L

Where:

A = 6.6826 dexametasone (sum of 4.3866 kg dexametasone and 3.0198 kg dexametasone natriumphosphate, equaling 2.296 kg dexamethasone) (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 (Pseudokirchneriella subcapitata) (ISO 8692, 1987) (Della Greca et al. 2004)*:*
ErC50 72 h (growth inhibition) > 100.0 mg/L

Crustacean (Daphnia magna):
Acute toxicity
EC50 24 h (immobilisation) > 100.0 mg/L (OECD 202) (Ciba-Geigy Project No. 830166)

Other ecotoxicity data:
Bacterial Respiration Inhibition:
EC_{50} 3 h > 320 mg/L (Inhibition of Oxygen Consumption by activated sludge, 87/302/EEC, Part C) (ECOTOXICOLOGY Report N 139 05)

PNEC derivation:
No PNEC can be calculated since there is not sufficient information on environmental toxicity available

Environmental risk classification (PEC/PNEC ratio)

Calculation of a risk ratio is not possible, as there is not sufficient environmental toxicity data available. Therefore, the following phrase is used: "Risk of environmental impact of dexametasone cannot be excluded, since there is not sufficient ecotoxicity data available."

Degradation

Biotic degradation

Ready degradability:
0 %, not readily biodegradable (OECD301E) (Ciba-Geigy, Project No. 83 01 65)
Justification of chosen degradation phrase:
As dexamethasone does not fulfil the criteria for ready biodegradability, the following phrase is chosen for degradation potential: ‘Dexamethasone is potentially persistent.’

Bioaccumulation

Partitioning coefficient:
$\log K_{ow}$ = 1.83 (method unknown) (Alcon Technical Report No. 090:38560:0796)
Justification of chosen bioaccumulation phrase:
As $\log K_{ow} < 4$, the following statement is used for Dexamethasone: ‘Dexmethasone has low potential for bioaccumulation.’

Excretion (metabolism)

Dexamethasone is eliminated from plasma with a half-life of 2.4-3.5 hours. The mean plasma clearance is 245 mL/min.
Within 24 hours 64% of a radioactive dose of 0.5-1.5 mg dexamethasone is excreted in the urine. Up to 36% of the dose is recovered in the urine in the form of the principal metabolite, 6β-hydroxyldexamethasone, and about 2% of the dose is found in the form of unchanged dexamethasone (Millicorten® Basic Drug Information, CIBA, 1994).

References

1. 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
2. Della Greca et al. 2004. Toxicity of prednisolone, dexamethason and their photochemical derivatives on aquatic organisms. Chemosphere 54, p. 629-637.
3. Ciba-Geigy, Project No. 830166, Final report: 26.5.1983 (report / full reference not available)
4. ECOTOXICOLOGY Report N 139 05 (report / full reference not available, including date)
5. Ciba-Geigy, Project No. 83 01 65, Final report: 28.4.1983 (report / full reference not available)
6. Alcon Technical Report No. 090:38560:0796 (report / full reference not available, including date)
7. Millicorten® Basic Drug Information, CIBA, October 19th, 1994.
8. Laboratories Limited, March 2009.

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:

PEC (µg/L) = $(A*10^{9}*(100-R))/(365*P*V*D*100) = 1.37*10^{-6} * A * (100-R) = 1.37*10^{-6} * 10.537* 100$
PEC = 0.00144 µg/L

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 = $10 *10^{6}$
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
EC_{50} 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 Kow < 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/information_requirements_en.htm
- 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 (CO_2) 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