FASS

Ciprofloxacin Villerton

MRx EF

Mylan Hospital

Infusionsvätska, lösning 2 mg/ml
(klar, fri från synliga partiklar)

Antibakteriellt kinolonderivat, fluorokinolon

Aktiv substans:
Ciprofloxacin

ATC-kod:
J01MA02

Läkemedel från Mylan Hospital omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Miljöinformationen för ciprofloxacin är framtagen av företaget Novartis för Ciloxan

Miljörisk: Användning av ciprofloxacin har bedömts medföra hög risk för miljöpåverkan.
Nedbrytning: Ciprofloxacin är potentiellt persistent.
Bioackumulering: Ciprofloxacin 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) = $(A*10^9*(100-R))/(365*P*V*D*100) = 1.5*10^{-6} * A * (100–R) = 1.5*10^{-6} * 2634.915$ kg * 100

PEC = 0.395 µg/L

Where:

A = 2634.915 kg ciprofloxacin base (21.005 kg ciprofloxacin, 2975.82 kg ciprofloxacin hydrochloride monohydrate, 58.815 kg ciprofloxacin hydrochlorid, 7.27 kg ciprofloxacin hydrogensulphate (total sold amount API in Sweden in year 2016, data from QuintilesIMS)). (For normalization of amounts of the various ciprofloxacin salt forms to ciprofloxacin base please refer to Appendix I)

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 = $9 *10^6$

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 (Mycrocystis aeruginosa) (OECD 201) (Halling-Sørensen, 2000)*:*

EC50 (endpoint not specified) = 0.005 mg/L
Green algae:
Selenastrum capricornutum (OECD 201) (Halling-Sørensen, 2000)*:*
EC50 (endpoint not specified) = 2.97 mg/L
Pseudokirchneriella subcapitata (OECD 201) (Martins, 2012)
EC50 96 h (growth inhibition) = 4.83 mg/L

Crustacean (Daphnia magna, giant waterflea*):*
Acute toxicity
EC50 48 h (immobilization) = 65.3 mg/L (OECD 202) (Martins, 2012)
Chronic toxicity
NOEC 21 days (size of neonates from first brood) = 1.8 mg/L (OECD 202 Part II) (Martins, 2012)
NOEC 28 days (reproduction) = 0.156 mg/L (OECD 211) (Zaleska-Radziwill, 2011)

Fish:
Acute toxicity (*Gambusia holbrooki*, Eastern mosquitofish)
LC50 96 h (lethality) > 60.0 mg/L (OECD 203) (Martins, 2012)
Chronic toxicity (*Lebistes reticulatus,* guppy)
NOEC 28 days (juvenile growth stimulation) = 0.78 mg/L (OECD 215) (Zaleska-Radziwill, 2011)

Other ecotoxicity data:
Bacterial respiration inhibition
EC_{50} = 0.61 mg/L (activated sludge respiration inhibition) (ISO 15522) (Halling-Sørensen, 2000)

PNEC derivation:
PNEC = 5.0 ng/L

The PNEC is based on the lowest EC50 / 1000, where 1000 is the assessment factor used if acute data for 3 trophic levels is available. The EC50 for growth inhibition in the cyanobacteria *Mycrocystis aeruginosa* 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 = 0.395 µg/L / 0.005 µg/L = 79, i.e. PEC/PNEC > 10 which justifies the phrase "Use of ciprofloxacin has been considered to result in high environmental risk."

Degradation

Biotic degradation

Ready degradability:

Not readily degradable (28 days; Measurement of biological oxygen demand according to the guidelines published by OECD). (Halling-Sørensen, 2000)

Justification of chosen degradation phrase:

Ciprofloxacin is not readily biodegradable. Therefore, the phrase 'Ciprofloxacin is potentially persistent' is chosen.

Bioaccumulation

Partitioning coefficient:

Log Kow = 1.24 (estimated with ACD Log P software (Advanced Chemical Development, Toronto, Canada) (Halling-Sørensen, 2000)

Justification of chosen bioaccumulation phrase:

Since log K_{ow} < 4, ciprofloxacin has low potential for bioaccumulation.

Excretion (metabolism)

Ciprofloxacin is eliminated by renal and non-renal mechanisms. The drug is partially metabolized in the liver by modification of the piperazinyl group to at least 4 metabolites. These metabolites, which have been identified as desethyleneciprofloxacin (M1), sulfociprofloxacin (M2), oxociprofloxacin (M3), and N-formylciprofloxacin (M4), have microbiologic activity that is less than that of the parent drug.
Ciprofloxacin and its metabolites are excreted in urine and feces. Unchanged ciprofloxacin is excreted in urine by both glomerular filtration and tubular secretion. Following oral administration of a single 250-, 500-, or 750-mg dose in adults with normal renal function, 15–50% of the dose is excreted in urine as unchanged drug and 10–15% as metabolites within 24 hours; 20–40% of the dose is excreted in feces as unchanged drug and metabolites within 5 days. Most, but not all, of unchanged ciprofloxacin in feces appears to result from biliary excretion. (Medicines Complete 2017).

References

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- B. Halling-Sørensen, H.-C. Holten Lützhøft, H.R. Andersen and F. Ingerslev. 2000. Environmental risk assessment of antibiotics: comparison of mecillinam, trimethoprim and ciprofloxacin. Journal of Antimicrobial Chemotherapy 46, Suppl. S1, 53-58
- N. Martins, R. Pereira, N. Abrantes, J. Pereira, F. Gonçalves, C. R. Marques. 2012. Ecotoxicological effects of ciprofloxacin on

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- M. Zaleska-Radziwill, M. Lebkowska, K. Affek, A. Zarzeczna. 2011. Environmental risk assessment of selected pharmaceuticals present in surface waters in relation to animals. Archives of Environmental Protection 37 (3), 31-42.
- MedicinesComplete © 2017 Royal Pharmaceutical Society. AHFS Drug Information. https://www.medicinescomplete.com/mc/ahfs/current/a388016.htı

Appendix I

21.005 kg ciprofloxacin
MW: 331.3 g/mol

2975.82 kg ciprofloxacin hydrochloride monohydrate
MW: 385.82 g/mol
→ 2975.82 kg / 385.82 g/mol * 331.3 g/mol = 2555.31 kg ciprofloxacin

58.815 kg ciprofloxacin hydrochlorid
MW: 367.8 g/mol
→ 58.815 kg / 367.8 g/mol * 331.3 g/mol = 52.98 kg

7.27 kg ciprofloxacin hydrogensulphate
MW: 428.364
→ 7.27 kg / 428.364 g/mol * 331.3 g/mol = 5.62 kg
SUM: 2634.915 kg ciprofloxacin base