

Sandimmun Neoral (Parallellimporterat)

Cross Pharma AB

Kapsel, mjuk 25 mg

Avregistreringsdatum: 2016-11-02 (Tillhandahålls ej)

Inga avvikelser.

Visa information om det parallellimporterade läkemedlet

Aktiv substans:

Ciklosporin

ATC-kod:

L04AD01

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

Läs mer om avregistrerade läkemedel

Miljöpåverkan

Miljöinformationen för ciklosporin är framtagen av företaget Novartis för Sandimmun Neoral®, Sandimmun®

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

Nedbrytning: Ciklosporin bryts ned i miljön.

Bioackumulering: Ciklosporin 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:

$$\text{PEC } (\mu\text{g/L}) = (A \cdot 10^9 \cdot (100 - R)) / (365 \cdot P \cdot V \cdot D \cdot 100) = 1.37 \cdot 10^{-6} \cdot A \cdot (100 - R) = 1.37 \cdot 10^{-6} \cdot 107.9739 \cdot 100$$

$$\text{PEC} = 0.0148 \mu\text{g/L}$$

Where:

A = 107.9739 kg (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

Algae (Desmodesmus subspicatus) (OECD201) (Ciba-Geigy Ecotoxicology Test No. 918247):

EC50 72 h (no information on endpoint available) > 100.0 mg/L

Crustacean (Daphnia magna):

Acute toxicity

EC50 48 h (immobilisation) = 20.2 mg/L (OECD202) (Ciba-Geigy Ecotoxicology Test No. 918248)

Fish:

Acute toxicity (*Oncorhynchus mykiss*, rainbow trout)

LC50 96 h (mortality) > 100.0 mg/L (OECD203) (Ciba-Geigy Ecotoxicology Test No. 918170)

Other ecotoxicity data:

Bacterial respiration inhibition

EC₅₀ 3h > 100.0 mg/L (activated sludge respiration inhibition) (OECD209) (Ciba-Geigy Ecotoxicology Test No. 918171)

PNEC derivation:

PNEC = 20.2 µg/L

PNEC (µg/L) = lowest EC₅₀/1000, where 1000 is the assessment factor used if three acute toxicity studies from three trophic levels are available. The immobilization of *Daphnia magna* has been used to derive the PNEC for ciclosporin.

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.0148 µg/L / 20.2 µg/L = 0.00073, i.e. PEC/PNEC ≤ 0.1 which justifies the phrase "Use of ciclosporin has been considered to result in insignificant environmental risk."

Degradation

Biotic degradation

Ready degradability:

84.0 % degradation in 28 days, readily biodegradable (OECD301B). (Ciba-Geigy Ecotoxicology Test No. 918172)

Justification of chosen degradation phrase:

Ciclosporin has passed the criteria for ready biodegradation. Therefore, it can be classified as Ciclosporin is degraded in the environment.

Bioaccumulation

Partitioning coefficient:

$\text{Log } P_{\text{ow}} = 2.92$ (experimentally determined, measured in octanol/water by centrifugal partition chromatography) (El Tayar et. al. 1993)

Justification of chosen bioaccumulation phrase:

As the octanol/water partition coefficient of ciclosporin is below 4, the following statement is chosen: Ciclosporin has low potential for bioaccumulation.

Excretion (metabolism)

Ciclosporin is extensively metabolised to more than 15 metabolites. The main site of metabolism is the cytochrome P450-dependent mono-oxygenase system in the liver, and the main pathways of metabolism consist of mono- and dihydroxylation and n-demethylation at various positions of the molecule. All metabolites identified so far contain the intact peptide structure of the parent compound, some possess weak immunosuppressive activity (up to one-tenth that of the unchanged drug). Elimination is primarily biliary, with only 6% of an oral dose excreted in the urine and with less than 1% in the unchanged form. (Novartis Core Data Sheet Sandimmun[®])

PBT/vPvB assessment

Ciclosporin has been found to be readily biodegradable and can therefore not be considered a potential PBT or vPvB substance.

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
- Ciba-Geigy Ecotoxicology Test No. 918247
- Ciba-Geigy Ecotoxicology Test No. 918248
- Ciba-Geigy Ecotoxicology Test No. 918170
- Ciba-Geigy Ecotoxicology Test No. 918171
- Ciba-Geigy Ecotoxicology Test No. 918172
- N. El Tayar et. al. 1993. Solvent-dependent conformation and hydrogen-bonding capacity of cyclosporin A: evidence from partition coefficients and molecular dynamics simulations. J. Med. Chem. 36, 3757-3764.
- Novartis Core Data Sheet Sandimmun[®] (ciclosporin), Version 1.1. 05 August 2014.