

Primperan[®]

Sanofi AB

Tablett 10 mg

Avregistreringsdatum: 2024-08-01 (Tillhandahålls ej) (vit, rund med skåra, 7 mm)

! M R F

Medel för behandling av nedsatt motilitet i mag-tarmkanalen samt mot illamående och kräkningar

Aktiv substans:

Metoklopramid

ATC-kod:

A03FA01

Läkemedel från Sanofi AB omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Metoklopramid

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

Nedbrytning: Metoklopramid är potentiellt persistent.

Bioackumulering: Metoklopramid har låg potential att bioackumuleras.

Detaljerad miljöinformation

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

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

$$\text{PEC} = 0.012 \mu\text{g/L}$$

Where:

A = 86.128 kg (total sold amount API in Sweden year 2022, data from IQVIA)

R = 0% removal rate (due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation)

$P = \text{number of inhabitants in Sweden} = 10 \cdot 10^6$

$V \text{ (L/day)} = \text{volume of wastewater per capita and day} = 200 \text{ (ECHA default) (Ref I)}$

$D = \text{factor of dilution of waste water by surface water flow} = 10 \text{ (ECHA default) (Ref I)}$

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

Algae (Pseudokirchneriella subcapitata)

$EC_{50} \text{ 72 h (growth rate)} = 35,6 \text{ mg/L} = 35\,600 \text{ }\mu\text{g/L}$

$NOEC \text{ 72 h (growth rate)} = 1,35 \text{ mg/L} = 1350 \text{ }\mu\text{g/L}$

Guideline: OECD 201

(Ref II)

Crustacean (Daphnia magna)

Acute toxicity

$EC_{50} \text{ 48 h (immobilisation)} = 84,3 \text{ mg/L} = 84\,300 \text{ }\mu\text{g/L}$

Guideline: OECD 202

(Ref III)

Fish (zebrafish embryos (Danio rerio))

Acute toxicity

$LC_{50} \text{ 96 h (mortality)} > 100 \text{ mg/L} = 100\,000 \text{ }\mu\text{g/L}$

Guideline: OECD 236

(Ref IV)

Other ecotoxicity data

$PNEC = 35,6 \text{ }\mu\text{g/L}$

e.g. $PNEC \text{ (}\mu\text{g/L)} = \text{lowest } EC_{50}/1000$, where 1000 is the assessment factor used.

EC_{50} for *Pseudokirchneriella subcapitata* has been used for this calculation since it is the most sensitive of the three tested species.

$35\,600 \text{ }\mu\text{g/L}/1000 = 35,6 \text{ }\mu\text{g/L}$

Environmental Risk Classification (PEC/PNEC ratio)

$PEC/PNEC = 0,012 \text{ }\mu\text{g/L}/35,6 \text{ }\mu\text{g/L} = 0,00033$

$PEC/PNEC \leq 0,1$ which justifies the phrase:

Use of metoclopramid has been considered to result in insignificant environmental risk.

Degradation

Biotic degradation

Ready degradability

0 % in 28 days

Guideline: OECD 301F

(Ref V)

Justification of chosen degradation phrase:

Metoclopramid is potentially persistent.

Bioaccumulation

Partition coefficient

Log P = 2.667 (experimentally derived, method unknown, pH unknown)

(Ref VI)

Justification of chosen bioaccumulation phrase:

Since $\log P < 4$, metoclopramide has low potential for bioaccumulation.

Excretion (metabolism)

The excretion takes place in the urine. About 85 % of the dose is eliminated within 72 hours, 20-30 % as unchanged metoclopramide and the remainder as sulphate or glucuronide conjugate, or as other metabolites. About 5% is excreted in the faeces via the bile.

(Ref VII)

References

- I. ECHA, European Chemicals Agency, 2008 Guidance on information requirements and chemical safety assessment.
<https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety->
- II. Sanofi, Internal Report: Metoclopramide Hydrochloride Monohydrate: Toxicity to *Pseudokirchneriella subcapitata* in an Algal Growth Inhibition Test. Report # 117731210. 2017
- III. Sanofi, Internal Report: Metoclopramide Hydrochloride Monohydrate: Acute Toxicity to *Daphnia magna* in a Static 48-hour Immobilisation Test. Report # 117731220. 2017
- IV. Sanofi, Internal Report: Metoclopramide Hydrochloride Monohydrate: Acute Toxicity to Zebrafish (*Danio rerio*) Embryos in a 96-hour Static Test. Report # 117731238. 2017
- V. Sanofi, Internal Report: Metoclopramide hydrochloride: Ready Biodegradability in a Manometric Respirometry. Report # 117731163. 2017
- VI. Metoclopramide, retrieved from DrugBank webpage 2021-04-22, find here
- VII. SmPC of Priperan, retrieved from SE MPA webpage 2021-04-22, find here