

**Primperan®****M****Sanofi AB**

Suppositorium 20 mg

Avregistreringsdatum: 2014-01-27 (Tillhandahålls ej) (vita)

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

**Aktiv substans:**

Metoklopramid

**ATC-kod:**

A03FA01

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

Läs mer om avregistrerade läkemedel

## 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 = number of inhabitants in Sweden =  $10 \cdot 10^6$

V (L/day) = volume of wastewater per capita and day = 200 (ECHA default) (Ref I)

D = factor of dilution of waste water by surface water flow = 10 (ECHA default) (Ref I)

### Predicted No Effect Concentration (PNEC)

## Ecotoxicological studies

*Algae (Pseudokirchneriella subcapitata)*

EC<sub>50</sub> 72 h (growth rate) = 35,6 mg/L = 35 600 µg/L

NOEC 72 h (growth rate) = 1,35 mg/L = 1350 µg/L

Guideline: OECD 201

(Ref II)

*Crustacean (Daphnia magna)*

Acute toxicity

$EC_{50}$  48 h (immobilisation) = 84,3 mg/L = 84 300 µg/L

Guideline: OECD 202

(Ref III)

*Fish (zebrafish embryos (Danio rerio))*

Acute toxicity

$LC_{50}$  96 h (mortality) > 100 mg/L = 100 000 µg/L

Guideline: OECD 236

(Ref IV)

*Other ecotoxicity data*

PNEC = 35.6 µg/L

e.g. PNEC (µg/L) = 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.

$35\,600\text{ µg/L}/1000 = 35.6\text{ µg/L}$

**Environmental Risk Classification (PEC/PNEC ratio)**

$PEC/PNEC = 0.012\text{ µg/L}/35.6\text{ µg/L} = 0.00033$

$PEC/PNEC \leq 0.1$  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>
- 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