

Flagyl®

Sanofi AB

Tablett 200 mg

Avregistreringsdatum: 2022-01-31 (Tillhandahålls ej) (vit, bikonvex, ca 10 mm, märkt "FLAGYL 200")

Specifikt medel mot anaeroba bakterier och vid trikomonas-, amöba- och giardiainfestation

Aktiv substans:

Metronidazol

ATC-kod:

P01AB01

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

M

Läs mer om avregistrerade läkemedel

Miljöpåverkan

Metronidazol

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

Nedbrytning: Metronidazol är potentiellt persistent.

Bioackumulering: Metronidazol har låg potential att bioackumuleras.

Detaljerad miljöinformation

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

$$PEC (\mu\text{g/L}) = (A \cdot 10^9 \cdot (100 - R)) / (365 \cdot P \cdot V \cdot D \cdot 100) = 1.5 \cdot 10^{-6} \cdot A \cdot (100 - R)$$

$$PEC = 0.204 \mu\text{g/L}$$

Where:

A = 1361.9 kg (total sold amount API in Sweden year 2019, 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 = $9 \cdot 10^6$

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

Cyanobacteria (Anabaena flos-aquae)

EC₁₀ 72 h (growth rate) = 13 500 µg/L

EC₅₀ 72 h (growth rate) > 95 200 µg/L

NOEC 72 h (growth rate) = 2 770 µg/L

Guideline: OECD 201

(Ref II)

Water flea, Daphnia magna:

Acute toxicity

EC₅₀ 48 h (inhibition of motility) > 100 000 µg/L

Guideline: OECD 202

(Ref III)

Chronic toxicity

NOEC 21 days (reduction in reproduction) = 250 000 µg/L

Guideline: OECD 211

(Ref IV)

Fish embryos (Danio rerio)

Acute toxicity

LC₅₀ 96 h (mortality) > 100 000 µg/L

Guideline: OECD 236

(Ref V)

Other ecotoxicity data:

PNEC = 1350 µg/L

The PNEC (µg/L) = 13 500/10 = 1350 µg/L

To calculate the PNEC from an anti-microbial effect study with *cyanobacteria*, a default assessment factor of 10 is applied to the EC₁₀. The EC₁₀ is preferred over the NOEC for PNEC derivation, even if the former is higher than the latter.

Environmental Risk Classification (PEC/PNEC ratio)

PEC/PNEC = $0.204/1350 = 0.00015$, i.e. $PEC/PNEC \leq 0.1$ which justifies the phrase

"Use of metronidazole has been considered to result in insignificant environmental risk"

Biodegradation

Ready degradability

Test results showed 1 % degradation in 28 days.

(OECD 301)

(Ref VI)

Justification of chosen degradation phrase:

Metronidazole failed to pass the ready degradation test, justifying the phrase: "Metronidazole is potentially persistent".

Bioaccumulation

Partitioning coefficient:

$\log P = -0.15$ (pH unknown, source ALOGPS)

(Ref VII)

Justification of chosen bioaccumulation phrase:

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

Excretion (metabolism)

Metronidazole is partially metabolised by oxidation and hydroxylation and is also conjugated with glucuronic acid. The active metabolite is hydroxymetronidazole.

Excretion of unchanged metronidazole and its metabolites occurs mainly via the urine. A small portion is eliminated via the bile.
(Ref VIII)

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: Metronidazole: Toxicity to *Anabaena flos-aque* in an Algal Growth Inhibition Test. Report # 127651218. 2018
- III. Sanofi, Internal Report: Metronidazole: Acute Toxicity to *Daphnia magna* in a Static 48-hour Immobilisation Test. Report # 127651220.2018
- IV. L. Wollenberger, B. Halling-Sørensen, K.O Kusk, Acute and chronic toxicity of veterinary antibiotics to *Daphnia magna*, Chemosphere, Volume 40, Issue 7, 2000, Pages 723-730
- V. Sanofi, Internal Report: Metronidazole: Acute Toxicity to Zebrafish (*Danio rerio*) Embryos in a 96-hour Static Limit Test. Report # 127651238.2018
- VI. Ings RMJ, Law GL, Parnell EW, 1966, The metabolism of metronidazole (1-2'-hydroxyethyl-2-methyl-5-nitroimidazole), Biochemical Pharmacology, 15, 515-519.
- VII. DrugBank - Metronidazole, retrieved from drugbank.com 2021-05-14, find here.
- VIII. SmPC of Flagyl 200 mg tablet, retrieved from SE MPA 2021-08-18, find here.