



## Orudis®

M R F

Sanofi AB

Kapsel, hård 50 mg

(vit 5,5×16,3 mm)

Antiflogistikum med analgetisk och antipyretisk effekt

**Aktiv substans:**

Ketoprofen

**ATC-kod:**

M01AE03

Läkemedel från Sanofi AB omfattas av Läkemedelsförsäkringen.

## Miljöpåverkan

### Ketoprofen

Miljörisk: Användning av ketoprofen har bedömts medföra låg risk för miljöpåverkan.

Nedbrytning: Ketoprofen är potentiellt persistent.

Bioackumulering: Ketoprofen har låg potential att bioackumuleras.

### Detaljerad miljöinformation

#### Environmental Risk Classification

#### *Predicted Environmental Concentration*

PEC is calculated according to the following formula:

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

$$\text{PEC} = 0.18 \text{ } \mu\text{g/l}$$

Where:

A = 1301.6 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)

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

V (L/day) = volume of wastewater per capita and day = 200 (Ref I)  
D = factor of dilution of waste water by surface water flow = 10 (Ref I)

### **Predicted No Effect Concentration (PNEC)**

#### *Ecotoxicological studies*

*Algae (*Pseudokirchneriella subcapitata*):*

EC<sub>50</sub> 72 h (growth rate): 30.2 µg/L

EC<sub>10</sub> 72 h (growth rate): 24.1 µg/L

NOEC 72 h (growth rate): 17.8 µg/L

Protocol: OECD 201

(Ref II)

*Crustacean (*Daphnia magna*):*

EC<sub>10</sub> 21 d (reproduction): 11200 µg/L

NOEC 21 d (reproduction): 9150 µg/L

Protocol: OECD 211

(Ref III)

*Fish (*Danio Rerio*):*

LC<sub>50</sub> 96 h (lethality): > 100000 µg/L

NOEC 96 h (lethality): > 100000 µg/L

Protocol: OECD 236

(Ref IV)

*Fish (*Danio Rerio*):*

LC<sub>10</sub> 28 days (lethality): 435 µg/L

NOEC 28 days (lethality): 93 µg/L

Protocol: OECD 210

(Ref V)

*Other ecotoxicity data:*

Lowest NOEC/10:

*Algae (*Pseudokirchneriella subcapitata*):*

NOEC 72 h (growth rate): 17.8 µg/L

PNEC: 17.8 µg/L/10 = 1.78 µg/L

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

PEC/PNEC: 0.18/1.78 = 0,10

0.1 < PEC/PNEC ≤ 1: Use of ketoprofen has been considered to result in low environmental risk.

#### **Degradation**

#### **Biodegradation**

*Ready degradability:*

Test showed 0% degradation in 29 days (protocol: ISO9439) (Ref VI)

*Justification of chosen degradation phrase:*

Ketoprofen fails to pass the ready degradation test according to OECD criteria, which justifies the phrase  
“Ketoprofen is potentially persistent”

**Bioaccumulation**

*Partition coefficient:*

Ketoprofen has low potential for bioaccumulation, as indicated by a log Kow of 1.65 at pH 7 (protocol: OECD 107)  
(Ref VII)

**Excretion**

Around 80% of an administered dose is excreted in the urine, mainly as a glucuronide metabolite (Ref VIII).  
Ketoprofen metabolites are not active (Ref IX).

**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-assessment>
- II. Sanofi Internal report: Ketoprofen: Toxicity to *Pseudokirchneriella subcapitata* in an Algal Growth Inhibition Test. OECD 201. Report 117651210 , February 2017.
- III. Sanofi Internal report: Influence to *Daphnia magna* in a Semi-Static Reproduction Test. OECD 211. Report 117651221, March 2017.
- IV. Sanofi internal report: Acute Toxicity to Zebrafish (*Danio rerio*) Embryos in a 96-hour Static Test. OECD 236. Report 117651238, February 2017
- V. Sanofi internal report: Ketoprofen: Toxicity to Zebrafish (*Danio rerio*) in an Early-Life Stage Test. OECD 210. Report 135531232, January 2019.
- VI. Internal report: Ketoprofen, Biodegradability test (1993)
- VII. Internal report: Ketoprofen, Octanol-water partition coefficient determination (1993)
- VIII. Miles S., 2007, Ketoprofen, *xPharm: The Comprehensive Pharmacology Reference*, p1-7
- IX. Williams R.L. and Upton R.A., 1988, The Clinical Pharmacology of Ketoprofen, *The Journal of Clinical Pharmacology*, 28 (issue supplement S1), p S13-S22