

**Invanz<sup>®</sup>**

**M R EF**

**MSD**

Pulver till koncentrat till infusionsvätska, lösning 1 g  
(vitt till benvitt pulver)

Antibiotikum av karbapenemtyp

**Aktiv substans:**

Ertapenem

**ATC-kod:**

J01DH03

Läkemedel från MSD omfattas av Läkemedelsförsäkringen.

Läkemedlet distribueras också av företag som inte omfattas av Läkemedelsförsäkringen, se Förpackningar.

## Miljöpåverkan

### Ertapenem

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

Nedbrytning: Ertapenem är potentiellt persistent.

Bioackumulering: Ertapenem har låg potential att bioackumuleras.

### Detaljerad miljöinformation

#### Environmental Risk Classification

#### *Predicted Environmental Concentration (PEC)*

PEC is calculated according to the following formula:

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

$$PEC = 0.0016 \mu\text{g/L}$$

Where:

A = 12 kg (total sold amount API in Sweden year 2021, data from IQVIA) (Ref. I).  
R = 0 % removal rate (worst case assumption)  
P = number of inhabitants in Sweden =  $10 \cdot 10^6$   
V (L/day) = volume of wastewater per capita and day = 200 (ECHA default) (Ref. II)  
D = factor for dilution of waste water by surface water flow = 10 (ECHA default) (Ref. II)

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

#### **Ecotoxicological studies**

*Green Algae (Pseudokirchneriella subcapitata)* (OECD 201) (Ref. III)

EC<sub>50</sub> 72 h (growth rate) > 51 mg/L

NOEC = 51 mg/L

*Blue-Green Algae (Anabaena flos-aquae)* (OECD 201) (Ref. IV)

EC<sub>50</sub> 72 h (growth rate) = 0.23 mg/L

NOEC = 0.13 mg/L

Crustacean, water flea (*Daphnia magna*) (U.S. EPA Methods for Measuring the Acute Toxicity of Effluents and Receiving Waters to Fresh Water and Marine Organisms, 1993) (Ref. V)

Acute toxicity

EC<sub>50</sub> 48 h (mortality) > 500 mg/L

NOEC > 500 mg/L

Crustacean, water flea (*Daphnia magna*) (OECD 211) (Ref. VI)

Chronic toxicity

NOEC 21 d (survival, growth, reproduction) = 82 mg/L

Non-toxic up to highest concentration tested

Fish, fathead minnow (*Pimephales promelas*) (U.S. EPA Methods for Measuring the Acute Toxicity of Effluents and Receiving Waters to Fresh Water and Marine Organisms, 1993) (Ref. V)

Acute toxicity

LC<sub>50</sub> 96 h (mortality) > 1000 mg/L

Fish, fathead minnow (*Pimephales promelas*) (OECD 210) (Ref. VII)

Chronic toxicity

NOEC 32 d (survival) = 2.5 mg/L

PNEC = 13 µg/L (130 µg/L / 10 based on the chronic NOEC for the blue-green algae with an assessment factor (AF) of 10)

#### **Environmental risk classification (PEC/PNEC ratio)**

PEC/PNEC =  $.0016/13 = 1.3 \cdot 10^{-4}$ , i.e. PEC/PNEC ≤ .1 which justifies the phrase "Use of ertapenem has been considered to result in insignificant environmental risk."

#### **Degradation**

##### **Biotic degradation**

Ready Biodegradation (OECD 301B) (Ref VIII)

4.7% to CO<sub>2</sub> in 28 days

Not readily biodegradable

### **Abiotic degradation**

*Hydrolysis* (US FDA 3.09) (Ref. V)

Half life = 15.3 days at pH 7, 25 °C

*Photolysis* (US FDA 3.10) (Ref. IV)

In photolytic studies conducted in accordance with US FDA "Environmental Assessment Technical Assistance Handbook, Document 3.10", ertapenem's experimental half-life is 4.73 days in water at pH = 8.3 maintained at 21°C and exposed to light for 16 hours per day. In aqueous media, the major degradate is formed by the hydrolysis of the beta-lactam ring.

*Justification of chosen degradation phrase:*

Ertapenem is slightly degradable in biological systems however does not meet the criteria for degradability. The phrase "Ertapenem is potentially persistent in the environment" is thus chosen.

### **Bioaccumulation**

*Partitioning coefficient* (Method Unknown) (Ref.V)

Measured  $\text{Log } K_{ow} = - 2.22$

*Justification of chosen bioaccumulation phrase:*

Since  $\text{log } K_{ow} < 4$ , the substance has low potential for bioaccumulation.

### **References**

- I. Data from IQVIA "Consumption assessment in kg for input to environmental classification - updated 2022 (data 2021)".
- II. ECHA, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment.  
[http://guidance.echa.europa.eu/docs/guidance\\_document/information\\_requirements\\_en.ht](http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.ht)
- III. EAG Laboratories, 2017. "Ertapenem: A 72-Hour Toxicity Test With the Freshwater Alga (*Pseudokirchneriella Subcapitata*)", Report 105p-122, Easton MD, 20 January 2017.
- IV. EAG Laboratories, 2017. "Ertapenem: A 72-Hour Toxicity Test With the Cyanobacteria (*Anabaena Flos-Aquae*)", Report 105p-123, Easton MD, 17 February 2017.
- V. Merck, 2017. "Environmental Quality Criteria Monograph for Ertapenem Sodium", 26 September 2017.
- VI. EAG Laboratories, 2017. "Ertapenem: A Semi-Static Life-Cycle Toxicity Test With the Cladoceran (*Daphnia Magna*)", Report 105a-227, Easton MD, 23 February 2017.
- VII. EAG Laboratories, 2017. "Ertapenem: A Fish Early Life Stage Toxicity Test With the Fathead Minnow (*Pimephales promelas*)", Report 105a-228a, Easton MD, April 2017.
- VIII. EAG Laboratories, 2016. "Ertapenem: Ready Biodegradability by the Carbon Dioxide Evolution Test Method", Report 105E-182, Easton MD, 6 Oct 2016.