

Invanz[®]

MR 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)

EC₅₀ 72 h (growth rate) > 51 mg/L

NOEC = 51 mg/L

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

EC₅₀ 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

EC₅₀ 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

LC₅₀ 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 CO₂ 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 $\log K_{ow} = -2.22$

Justification of chosen bioaccumulation phrase:

Since $\log K_{ow} < 4$, 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
- 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.