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Environmental Risk Assessment
KEPPRA®

Summary

The PEC:PNEC ratios indicate that levetiracetam is unlikely to be a concern for the aquatic environment and the risk is classified at an insignificant level.

environment or the sewage treatment plant.

Levetiracetam is not readily biodegradable.

Levetiracetam is unlikely to bioaccumulate to any significant extent (Kow<1000).

Levetiracetam is unlikely to persist in water-bodies or accumulate in sediment systems.

PEC – Predicted Environmental Concentration

PEC=0,015 mg/L

$$PEC_{SURFACE\ WATER} = \frac{Dose_{A.I.} * F_{PEN}}{WASTEW_{INH} * Dilution}$$

Where,

- DoseA.I.: Maximum daily dose of active ingredient consumed per inhabitant (3000 mg),
- FPEN: Market penetration factor (Default = 0.01, i.e. 1%),
- WASTEWINH: Amount (litres) of wastewater per inhabitant per day (Default = 200 L*inh-1*d-1)
- Dilution: Dilution factor (Default = 10)

PNEC – Predicted No-Effect Concentration

PNEC=0,313 mg/L

Chronic toxicity studies have been performed for species from three trophic levels of the aquatic compartment following OECD guidelines which are universally accepted.

The PNEC is derived from the lowest NOEC (No Observed Effect Concentration) measured which is 3,13 mg/L for Pimephales promelas exposed to levetiracetam. The NOEC is divided by 10 as per EMA guidelines to obtain a PNEC=0,313 mg/L.

Environmental Risk Level – PEC/PNEC ratio

PEC/PNEC = 0,015/0,313 = 0,0479

The PEC/PNEC ratio is below 0,1. The proposed use of levetiracetam is therefore considered unlikely to represent an unacceptable risk to water and the risk is classified at an insignificant level.

Additional Data

The most important and widely accepted indication of bioaccumulation potential is a high value of the partition coefficient, log Kow (log Dow), and it is accepted that values of log Kow greater or equal to 3 indicate that the substance may bioaccumulate. For levetiracetam the measured logDow is -0.64 (at pH 7.4). This is below 3 and suggests that the potential for bioaccumulation of levetiracetam in aquatic organisms is likely to be minimal.

A ready biodegradation test was conducted in accordance with OECD test guideline 301B (CO2 evolution test) (Reference 2). Levetiracetam was not readily biodegradable within the test system (e.g. <60% degradation over 10 days) and was not considered to have inhibited microbial activity, as confirmed by the toxicity control.