



Environmental Risk Assessment BRIVIACT®

Summary

Brivaracetam is not readily biodegradable.

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

Brivaracetam is not expected to bioaccumulate to any significant extent ($K_{ow} < 1000$).

Brivaracetam does not persist in water-sediment systems, and is degraded to one extractable metabolite and several polar metabolites.

PEC – Predicted Environmental Concentration

PEC=0,001 mg/L

$$PEC_{\text{SURFACE WATER}} = \frac{\text{Dose}_{\text{A.I.}} * F_{\text{PEN}}}{\text{WASTEWINH} * \text{Dilution}}$$

Where,

- DoseA.I.: Maximum daily dose of active ingredient consumed per inhabitant (200 mg),
- F_{PEN}: 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=1 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 10 mg/L for *Pimephales promelas* exposed to brivaracetam. The NOEC is divided by 10 as per EMA guidelines to obtain a PNEC=1 mg/L.

Environmental Risk Level – PEC/PNEC ratio

$PEC/PNEC = 0,001/1 = 0,001$

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

Additional Data

The octanol-water partition coefficient (POW) was determined by the HPLC method (OECD Guideline 117) at neutral pH to be equivalent to 29 (Log POW = 1.5). This indicates that brivaracetam is unlikely to bioaccumulate. A PBT assessment and an evaluation of the bioconcentration factor is therefore not required.

A ready biodegradation test in accordance with OECD Guideline 301 B (CO₂ evolution test/modified Sturm test) showed that brivaracetam was not readily biodegradable within the test system. The substance did not inhibit microbial activity, as confirmed by the toxicity control.

The adsorption coefficient (KOC) was determined by the HPLC method (OECD Guideline 121) to be < 20.9 (Log KOC < 1.32). Brivaracetam is therefore unlikely to partition extensively to sewage sludge and will remain predominantly in the aqueous phase. An assessment of the fate and effects in the terrestrial compartment is not required based on this information. A groundwater assessment was however performed.

