Overall review - Ropivakain

Revision date: 2022-08-23 17:38:01

Manufacturer: Fresenius Kabi

Substance: Ropivakain

Overall review: **No remark**

Review of proposed Fass text

Environmental risk

Användning av ropivakain har bedömts medföra försumbar risk för miljöpåverkan. / Use of [name of the substance] has been considered to result in insignificant environmental risk.

Review: **No remark**

Degradation

Ropivakain bryts ned långsamt i miljön. / [Name of the substance] is slowly degraded in the environment

Review: **No remark**

Bioaccumulation

Ropivakain har låg potential att bioackumuleras. / [Name of the substance] has low potential for bioaccumulation.

Review: **No remark**

PBT

Review:

Other comments

Review:

Proposed Fass text

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

In order to normalize the different ropivacaine varieties on the active ingredient ropivacaine, all sales volumes are adjusted to the molecular weight of ropivacaine.

Ropivacaine variety

Molecular weight (g/mol)

Tonnage conversion factor

Ropivacaine

274,4

1

Ropivakaine hydrochloride, water free

310,87

1,13

Ropivacaine hydrochloride monohydrate

328,9

1,20

PEC is calculated according to the following formula:

PEC (µg/L) = $(A*10^9*(100-R))/(365*P*V*D*100) = 1.37*10^{-6}*18,45*(100-0)$

Where:

A = 18,45 kg ropivacaine as the total of 19,30 kg ropivacaine hydrochloride and 1,66 ropivacaine hydrochloride monohydrate all normalized to ropivacaine molecular weight (total sold amount API in Sweden year 2020, data from IQVIA).

R = 0 % removal rate (due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation) = 0 if no data is available.

P = number of inhabitants in Sweden = $10 *10^6$

V (L/day) = volume of wastewater per capita and day = 200 (ECHA default) (Ref. 1)

D = factor for dilution of waste water by surface water flow = 10 (ECHA default) (Ref. 1)

PEC = **0,00253 µg/L**

According to the European Medicines Agency guideline on environmental risk assessment of medicinal products (EMA/CHMP/SWP/4447/00), use of Ropivacaine is unlikely to represent a risk for the environment, because the predicted environmental concentration (PEC) is below the action limit 0.01 µg/L.

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies (Ref. 3)

Green alga *(Pseudokirchneriella subcapitata)* growth inhibition test (guideline OECD 201)

EC_{50} 72 h (growth rate) = 59 mg/L

Daphnia magna, (guideline OECD202)

Acute toxicity

EC_{50} 48 h (immobility) = 34 mg/L

Zebra fish, (*Danio rerio*), (guideline OECD203)

Acute toxicity

$LC5_0$ 96 h (mortality) = 38 mg/L

Based on the most sensitive acute species; *Daphnia magna* 48h LC50 of 34 mg/L (equivalent to 34000 µg/L) and an assessment factor of 1000 in accordance with ECHA guidance (Ref. 1).

PNEC = 34000 µg/L /1000 = 34 µg/L

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = **0,00253** / 34 = **7,4X10^{-5}** , PEC/PNEC ≤ 1 which justifies the phrase "Ropivacaine would have insignificant risk to the environment.

Degradation

Aerobic biodegradation (ISO 7827-1984 (E))

Percentage Dissolved Organic Carbon (DOC) removal after 28 days 0%

Not readily biodegradable (Ref. 3).

Bioaccumulation

LogP = 2,90 (Ref 2)

Since log P < 4 at pH 7, the substance has low potential for bioaccumulation.

References:

1. ECHA, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment.http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm

2. PubChem 2022-01-22, https://pubchem.ncbi.nlm.nih.gov/compound/175805

3. Environmental Risk Assessment Data/ Ropivacaine Hydrochloride /AstraZeneca