FASS

Primovist

MRx EF

Bayer

Injektionsvätska, lösning i förfylld spruta 0,25 mmol/ml
(Klar, färglös till svagt gul lösning fri från synliga partiklar.)

Paramagnetiskt kontrastmedel

Aktiv substans:
Gadoxetinsyra

ATC-kod:
V08CA10

Läkemedel från Bayer omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Gadoxetinsyra

Miljörisk: Användning av gadoxetinsyra har bedömts medföra försumbar risk för miljöpåverkan.
Nedbrytning: Gadoxetinsyra är potentiellt persistent.
Bioackumulering: Gadoxetinsyra har låg potential att bioackumuleras.

Detaljerad miljöinformation

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

PEC (µg/L) = $(A*10^9*(100-R))/(365*P*V*D*100) = 1.37*10^{-6}$ *A*(100-R) = 0.0021 µg/L

Where:

A = 14.94 kg (total sold amount API in Sweden year 2021, data from IQVIA / LIF).

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) (Reference I)

D = factor for dilution of wastewater by surface water flow = 10 (ECHA default) (Reference I)

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

*Algae (*green algae, *Desmodesmus subspicatus):*

E_rC_{50} 72 h (growth rate) = 308 mg/L, NOEC 72 h (growth rate) = 250 mg/L. Guideline OECD 201. (Reference II)

Crustacean (waterflea, *Daphnia magna):*

Acute toxicity

EC_{50} 48 h (immobilization) ≥ 100 mg/L. Guideline OECD 202. (Reference III)

*Fish (*Rainbow trout*, Oncorhychus mykiss):*

Acute toxicity

LC_{50} 96 h (survival) ≥ 1000 mg/L. Guideline FDA TAD 4.11. (Reference IV)
The PNEC was calculated based on the acute aquatic toxicity data since there is insufficient data on chronic aquatic toxicity. The PNEC was calculated by division of the lowest effect leve (EC_{50} or LC_{50})of the most sensitive taxonomic group considering an appropriate assessment factor (AF). The most sensitive taxonomic group were crustaceans and the lowest effect level was reported as EC_{50} ≥ 100 mg/L. The regulatory default standard AF of 1000 was used, which is applicable when there are acute aquatic toxicity studies representing the three trophic levels (algae, crustaceans, and fish).
PNEC = 100 mg/L / 1000 = 0.1 mg/L = 100 µg/L

Environmental risk classification (PEC/PNEC ratio)

The risk quotient PEC/PNEC was calculated with 0.0021 µg/L / 100 µg/L = 0.000021.
A risk quotient ≤ 0.1 for gadoxetic acid qualifies for the phrase "Use of gadoxetic acid has been considered to result in insignificant environmental risk."

Degradation

Biotic degradation

Ready degradability:
Gadoxetic acid was assessed for ready biodegradation according to test method OECD 301E. Municipal sewage sludge was used, and the test item was tested at 20 mg/L DOC. The study was fully valid

as the reference substance was degraded by 96 % already on day 5 and up to 100 % at day 28. The toxicity control showed no toxicity to the microbial community.
The study resulted with 0 % biodegradation in 28 days. Guideline OECD 301E. (Reference V)

Abiotic degradation

Hydrolysis:
Gadoxetic acid was found to be stable at environmentally relevant pH values of 5, 7, and 9. Guideline FDA TAD 3.09. (Reference VI)
Justification of chosen degradation phrase:
Gadoxetic acid is not readily biodegradable and resistant to hydrolysis, which qualifies for the phrase “Gadoxetic acid is potentially persistent”.

Bioaccumulation

Partitioning coefficient:
The log D_{ow} was reported with -4.9 at pH 7. Guideline OECD 107. (Reference VI)
Justification of chosen bioaccumulation phrase:
Due to the log D_{ow} well below 4 gadoxetic acid is not considered bioaccumulative which qualifies for the phrase “Gadoxetic acid has low potential for bioaccumulation”.

Excretion (metabolism)

Gadoxetic acid is not metabolized and excreted as parent compound into the environment. (Reference VII)

References

I. Guidance on information requirements and Chemical Safety Assessment Chapter R.16: Environmental exposure assessment. V3.0, Feb. 2016.
II. Growth inhibition test of ZK139834 on the green algae desmodesmus subspicatus. Schering AG, Experimental Toxicology. Report no. AY78, Study no. TXST19970088.
III. Acute toxicity test with gadoxetic acid, disodium (ZK139834) with Daphnia magna. Report no. AS28, study no. TXST19970140.
IV. Acute toxicity test with gadoxetic acid, disodium with the rainbow trout. Schering AG, Experimental Toxicology. Report no. AM34, study no. TX95303.
V. Study on the biodegradability of with gadoxetic acid, disodium in the modified OECD Screening Test. Report no. AT67, study no. TXST19970217.
VI. Report on the physic-chemical properties of Gd-EOB-DTPA (ZK139834). Schering AG, General Physical Chemistry. Report no. L493, study no.93/128.
VII. Excretion and biodistribution of ZK 139834 after single Intravenous Injection in the rat 1 and 7 days p.i. Schering AG, Forschung Kontrastmittel für Kernspintomographie. Report no. A752, study no. KM 92285.