FASS

Gadovist®

Bayer

Injektionsvätska, lösning i förfylld spruta/cylinderampull 1 mmol/ml
(klar, färglös till blekt gul lösning)

Paramagnetiskt kontrastmedel för magnetisk resonanstomografi (MRT)

Aktiv substans:
Gadobutrol (vattenfri)

ATC-kod:
V08CA09

Läkemedel från Bayer omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Gadobutrol (vattenfri)

Miljörisk: Användning av gadobutrol (vattenfri) har bedömts medföra försumbar risk för miljöpåverkan.
Nedbrytning: Gadobutrol (vattenfri) är potentiellt persistent.
Bioackumulering: Gadobutrol (vattenfri) 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) = $(A*10^{9}*(100-R))/(365*P*V*D*100) = 1.37*10^{-6}*A*(100-R)$
PEC = 0.00967 µg/L

Where:
A = 70.61 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 (Desmodesmus subspicatus)

NOEC 72 h (growth rate) = 2,062 µg/L (guideline OECD 201) (Reference II)*:*

Crustacean (Daphnia magna):

Acute toxicity

EC_{50} 48 h (immobilization, reproduction) ≥ 1,000 µg/L (guideline OECD 202) (Reference III)

Chronic toxicity

NOEC 21 days (immobilization, reproduction) ≥ 1,000 µg/L (guideline OECD 211) (Reference IV)

Fish (Danio rerio, Pimephales promelas):

Acute toxicity (*Danio rerio*)

LC_{50} 96 h (mortality) ≥ 100 µg/L (guideline OECD 203) (Reference V)

Chronic toxicity (Pimephales promelas)

NOEC 28 days (hatching, mortality growth) ≥ 1,000 µg/L (guideline OECD 210) (Reference VI)

Microorganisms

MIC <1-10 d (respiration inhibition) ≥ 1,000,000 µg/L (FDA TAD 4.02). (Reference VII)
The PNEC was calculated by division of the NOEC of the most sensitive taxonomic group with an assessment factor (AF). The most sensitive taxonomic group was crustaceans and fish, and both NOEC were reported with ≥ 1,000 µg/L. The regulatory default standard AF of 10 was used, which is applicable when there are chronic aquatic toxicity studies representing the three trophic levels (algae, invertebrates, and fish).
PNEC = 1,000 µg/L / 10 = 100 µg/L

Environmental risk classification (PEC/PNEC ratio)

The risk quotient PEC/PNEC = 0.00967 µg/L / 100 µg/L = 0.000097.

Justification of chosen environmental risk phrase:

With a risk quotient ≤ 0.1 substance gadobutrol anhydrous qualifies for the phrase “Use of gadobutrol anhydrous has been considered to result in insignificant environmental risk”.

Degradation

Biotic degradation

Ready degradability:

The aerobic biodegradability of gadobutrol in water was investigated in a modified CO_2-evolution test over 28 days, which was preceded by a pre-adaptation period of 14 days. At the end of the incubation, there was a slight increase of the Gd concentration in the sediment that was supposed to be related to the introduced substance. Gadobutrol is a contrast agent and these are known to be stable in the environment.

The study resulted with 4 % biodegradation in 28 days (guideline FDA TAD 3.11). (Reference VIII)

Abiotic degradation

Hydrolysis:

Gadobutrol is hydrolytically stable (guideline FDA TAD 3.09). (Reference IX)

Justification of chosen degradation phrase:
Gadobutrol anhydrous is not readily biodegradable and resistant to hydrolysis, which qualifies for the phrase “Gadobutrol anhydrous is potentially persistent”.

Bioaccumulation

Partitioning coefficient:
Log D_{ow} = -5.4 at pH 7 (guideline FDA TAD 3.02). (Reference X)

Justification of chosen bioaccumulation phrase:
Due to the log D_{ow} < 4 gadobutrol anhydrous is considered bioaccumulative which qualifies for the phrase “Gadobutrol anhydrous has low potential for bioaccumulation”.

References

I. 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
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.htm
III. Growth inhibition test of Gadobutrol on the green algae *Chlorella vulgaris*. Nonclinical Drug Safety, Schering AG, Report no. AM32, Study no. TX96038 (1996).
IV. Acute immobilization test of gadobutrol with *Daphnia magna*. Experimental Toxicology, Schering AG, Report no. AK12, Study no. TX94.066 (1994).
V. Reproduction study of Gadovist® (ZK 135079) in *Daphnia magna*. Nonclinical Drug Safety, Bayer Schering Pharma AG, Report no. A30908, Study no. TXST20050144 (2005).
VI. Acute toxicity of Gadovist® (ZK 135079) to the Zebrafish *Danio rerio*. Nonclinical Drug Safety, Bayer Schering Pharma AG, Report no. A29954, Study no. TXST20050265 (2005).
VII. ZK135079: Early life-stage toxicity test with fathead minnow (*Pimephales promelas*) under flow-through conditions. Nonclinical Drug Safety, Bayer Schering Pharma AG, Report no. A51566, study no. T3078909EXT; Springborn Smithers study no.1121.003.122 (2005)
VIII. Microbial growth inhibition test of gadobutrol with *Pseudomonas putida, Azotobakter beijerinckii, Aspergillus niger, Chaetomium globosum*, and *Nostoc ellipsosporum*. Schering AG, Experimental Toxicology, Report no. AB91, Study no. TX94.084 (1994)
IX. Study of aerobic biodegradation of gadobutrol. Schering AG, Experimental Toxicology, Report no. AC43, Study no. TX94.064 (1994).
X. The rate of hydrolysis of gadobutrol (ZK 135079). Schering AG, General Physical Chemistry, Report no. L391, study no. 94/070 (APC), (1994)