FASS

SIFROL®

Boehringer Ingelheim

Depottablett 2,1 mg

(Tillhandahålls ej) (vita till benvita, ovala och har kod inpräglad (kod P4) på ena sidan och företagssymbol på andra sidan)

Dopaminagonist, medel vid Parkinsons sjukdom

Aktiv substans:

Pramipexol

ATC-kod:

N04BC05

Läkemedel från Boehringer Ingelheim omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Pramipexol

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

Detaljerad miljöinformation

Predicted Environmental Concentration (PEC):

PEC is calculated according to the following formula:

PEC (µg/L) = $(A*10^{9}*(100-R))/ (365*P*V*D*100) = 1.5*10^{-4}*A$ = 0,0008 µg/L

Where:
A = 5,3951 kg pramipexol (corresponding to 7,6634 kg pramipexoldihydrokloridmonohydrat total sold amount API in Sweden year 2021, data from IQVIA)
R = 0 % removal rate
P = number of inhabitants in Sweden = $9*10^{6}$
V (L/day) = volume of wastewater per capita and day = 200 (ECHA default) (Ref I)
D = factor for dilution of waste water by surface water flow = 10 (ECHA default) (Ref I)

Predicted No Effect Concentration (PNEC):

Ecotoxicological studies

Green alga (*Desmodesmus subspicatus*) (OECD 201) (Ref II):
EC50 72 h (yield) = 26 mg/L
NOEC 72 h (yield) = 1.9 mg/L
EC50 72 h (biomass) = 32 mg/L
NOEC 72 h (biomass) = 4.1 mg/L
EC50 72 h (growth rate) = 240 mg/L
NOEC 72 h (growth rate) = 1.9 mg/L

Water-flea (*Daphnia magna*) (OECD 202) (Ref III):

EC50 48 h (immobilization) =70 mg/L
NOEC 48 h (immobilization) = 25 mg/L

Zebra fish (*Danio rerio*) (OECD 203) (Ref IV):
LC50 96 h (mortality) > 100 mg/L (= highest concentration tested)
NOEC 96 h (mortality) = 100 mg/L (= highest concentration tested)

In accordance with the European Technical Guidance Document, the EC50 based on algal growth rate is the more reliable endpoint than the EC50 based on algal biomass. Thus, for comparison with the other species the EC50 based on algal growth rate was considered. With respect to the acute effect studies with the different species, daphnia was the most sensitive species. An assessment factor of 1000 was used for calculation of the PNEC.

PNEC = 70 mg/L / 1000 = 0.07 mg/L = 70 µg/L

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0,0008 / 70 = $1.0*10^{-5}$

Conclusion: PEC / PNEC < 0.1 which justifies the phrase “Use of pramipexole has been considered to result in insignificant environmental risk”.

Degradation

Aerobic degradation (US-FDA, TAD 3.11) (Ref V)
3.5% mineralization in 28 days
80% primary degradation in 28 days (estimated 50% degradation in 17 days)

Aquatic photodegradation half-life (Ref VI)

pH 5 = 346 hours
pH 7 = 55,5 hours
pH 9 = 33,1 hours

Justification: Pramipexole is degraded photolytically over the range of pH likely to be encountered in the environment indicating that it is readily degraded. However although the aerobic degradation results indicate that significant biodegradation did occur, as 80% of the compound was degraded during the test period, significant mineralization did not occur and pramipexole did not pass the 10 day criteria. The phrase “Pramipexole is potentially persistent” is therefore used.

Bioaccumulation

Partitioning coefficient (OECD 107) (Ref VII):
pH 5 : log D = -2,9
pH 7 : log D = -1.0
pH 9 : log D = 0.7

Justification: Since log D < 4 at pH 7, “Pramipexole has low potential for bioacculumation”.

Excretion / metabolism

Pramipexole is metabolised in man only to a small extent and renal excretion of unchanged pramipexole is the major route of elimination and accounts for about 80% of dose. Approximatly 90% of a 14C-labelled dose is excreted through the kidneys while less than 2% is found in the faeces (Ref VIII).

References

I. ECHA, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment. Chapter R.10: Characterization of dose [concentration]-response for environment. http://echa.europa.eu/documents/10162/13632/information_requi
II. Boehringer Ingelheim GmbH internal report U05-0226, 2005
III. Boehringer Ingelheim GmbH internal report U05-0219, 2005
IV. Boehringer Ingelheim GmbH internal report U05-0220, 2005
V. Boehringer Ingelheim GmbH internal report U95-0203, 1995
VI. Boehringer Ingelheim GmbH internal report U96-0120, 1996
VII. Boehringer Ingelheim GmbH internal report U06-0010, 2005
VIII. Boehringer Ingelheim GmbH internal report U92-0018, 1991