FASS

EDURANT

Janssen

Filmdragerad tablett 25 mg
(Vit till benvit, filmdragerad, rund, bikonvex tablett med en diameter på 6,4 mm märkt "TMC" på den ena sidan och "25" på den andra sidan.)

Antiviralt medel för systemisk användning, NNRTI

Aktiv substans:
Rilpivirin

ATC-kod:
J05AG05

Läkemedel från Janssen omfattas av Läkemedelsförsäkringen.
Läkemedlet distribueras också av företag som inte omfattas av Läkemedelsförsäkringen, se Förpackningar.

Miljöpåverkan

Rilpivirin

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

Detaljerad miljöinformation

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

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

PEC = 0.0009055837 µg/L

Where:

A = total actual API sales in Sweden for the most recent year 6.6101 kg (total sold amount API in the most recent sales data for Sweden (2022) was distributed by IQVIA in 2023)

R = 0

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 (*Scenedesmus subspicatus*) (guideline e.g. OECD 201):
Algal growth inhibition test with the green algae [Reference II]:

$E\gamma C_{50}$ 72 h (yield) = > 0.022 mg/L
NOECγ (yield) = > 0.022 mg/L
E_rC_{50} 72 h (growth) = > 0.022 mg/L
$NOEC_r$ (growth) = > 0.022 mg/L

The 72-hour NOEC was determined to be > 22 µg/L, since up to and including this test concentration the growth rate and yield of the algae after 72 hours were not significantly lower than in the solvent control.

Crustacean (Daphnia magna) (water-flea) (guideline e.g. OECD 211):
Acute toxicity

No data available

Chronic toxicity
Reproduction test with water-flea (*Daphnia Magna*) [Reference III]:
NOEC 21 days = > 0.032 mg/L

Rilpivirine had no toxic effects on survival and reproduction of *Daphnia magna* after the exposure period of 21 days up to the highest test concentration.

Fish:
Acute toxicity
No data available

Chronic toxicity

Fish early life stage test with Zebra fish (*Brachydanio rerio*) (guideline e.g. OECD 210) [Reference IV]:
NOEC 28 days = > 0.020 mg/L

The NOEC was determined to be the test concentration of 20 µg/L, since up to and including this test concentration no toxic effect was observed on the eggs, larvae or fish. The overall LOEC was determined to

be >20 µg/L. Thus Rilpivirine had no toxic effects on the early life stages of zebra fish up to its water solubility under the conditions of the test.

Other ecotoxicity data:
Activated sludge respiration inhibition test (guideline e.g. OECD 209) [Reference V]:

EC_{50} 3h = could not be calculated but were clearly higher than 1000 mg/L
NOEC 3h = > 1000 mg/L

Rilpivirine had no significant inhibitory effect (≤15%) on the respiration rate of activated sludge after the incubation period of 3 hours at the limit test concentration of 1000 mg/L.

PNEC (µg/l) = lowest NOEC/10, where 10 is the assessment factor used. NOEC for the species Zebra fish (*Brachydanio rerio*) of > 20 µg/L has been used for this calculation since it is the most sensitive of the three tested species.

PNEC = 20 µg/L / 10 = 2 µg/L

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.0009055837 / 2 = 0.00045279185 i.e. PEC/PNEC ≤ 0.1

Conclusion for environmental risk:
Use of Rilpivirine has been considered to result in insignificant environmental risk.

Degradation
Biotic degradation
Ready biodegradation
Rilpivirine Hydrochloride: The test item attained 5% biodegradation after 28 days and therefore cannot be considered to be readily biodegradable under the strict terms and conditions of OECD Guideline No. 301B (Reference IX).

Simulation studies:

Aerobic degradation in aquatic sediment systems:
Rilpivirine was investigated for its aerobic degradation in a 100-day aquatic sediment test, according to OECD 308 [Reference VIII]:

The route and rate of degradation of Rilpivirine in two aquatic systems (river and pond) under aerobic conditions were investigated at 20 °C in the dark.
The rates of dissipation (DT50, DT90) of Rilpivirine from the water phase and the entire system were calculated using first order kinetics and the Origin calculation software. All calculated DT50 and DT90 values are summarized in the following table:

System	Water*		Total system	
	DT_{50} [days]	DT_{90} [days]	DT_{50} [days]	DT_{90} [days]
River	1.3	4.2	307	>1 year
Pond	1.2	4.1	321	>1 year

Note: Calculated by applying first-order kinetics.
*: Distribution of the test item into the sediment

The majority of the radioactivity found in the sediments was extractable, with values up to 90.0% of applied radioactivity for the river and 89.7% for the pond system. Non-extractable residues accounted for up to 12.7% of applied radioactivity for the river and 14.4% for the pond system throughout the study. Organic matter fractionation of the bound residues showed that the majority of the radioactivity was associated with the insoluble fraction (humin).

Radioactive carbon dioxide increased slightly from day 28 onwards but not exceed a mean amount of 1.2% in both systems. No other organic volatile compounds were formed at any time point during the study (<0.1% of applied).

A few minor metabolites were formed in the sediments, but none individually exceeded 3% of the applied radioactivity in either aquatic system.
In aerobic aquatic systems, Rilpivirine rapidly dissipated from the water phase by adsorption to the sediment. Once in the sediment, Rilpivirine was only slowly degraded. Some 14CO2 production and the formation of bound residues were observed.

Conclusion for degradation:
Rilpivirine is potentially persistent.

Abiotic degradation
Hydrolysis: -
Photolysis: -

Bioaccumulation
Partition coefficient octanol/water:
The partition coefficient octanol/water was determined using guideline OECD 123. [Reference VI]
Log Pow= 4.66 at 25°C using the slow stirring method.
pH = min/6.98 – max 8.76

Bioconcentration factor (BCF):

The bioconcentration and depuration characteristics of Rilpivirine in the Rainbow trout (Oncorhynchus mykiss) in a flow through system were examined according to OECD 305 [Reference VII].

BCF_{low} dose = 137.2

BCF_{high} dose = 125.6

The BCF –values indicate that Rilpivirine did not bioaccumulate in the rainbow trout.

Conclusion for bioaccumulation: Rilpivirine has low potential for bioaccumulation.

Excretion (metabolism)

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PBT/vPvB assessment

	PBT-criteria	Results for Rilpivirine
Persistence	Half-life in freshwater: DT_{50} > 40 days Half-life in sediment: DT_{50} > 120 days	DT50 total system - river 307 days - pond 321 days
Bioaccumulation	BCF > 2000	BCF_{low} dose = 137.2 BCF_{high} dose = 125.6
Toxicity	Chronic NOEC < 10 µg/L	$NOEC_{algae}$ = > 0.022 mg/L $NOEC_{daphnia}$ = > 0.032 mg/L $NOEC_{fish}$ = > 0,020 mg/l

Conclusion for PBT-assessment: Rilpivirine should not be regarded as PBT/vPvB substance.

References

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