

Aprovel

MR F_f

Sanofi AB

Tablett 75 mg

(Tillhandahålls ej) (vit till gråvit, bikonvex, oval med ett hjärta på en sida och 2771 på den andra)

Angiotensin II-antagonist

Aktiv substans:

Irbesartan

ATC-kod:

C09CA04

Läkemedel från Sanofi AB omfattas av Läkemedelsförsäkringen.

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

Miljöpåverkan

Irbesartan

Miljörisk: Användning av irbesartan har bedömts medföra försumbar risk för miljöpåverkan.

Nedbrytning: Irbesartan bryts ned långsamt i miljön.

Bioackumulering: Irbesartan har låg potential att bioackumuleras.

Detaljerad miljöinformation

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

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

$$PEC = 0.184 \mu\text{g/L}$$

Where:

A = 1342.937 kg (total sold amount API in Sweden year 2022, data from IQVIA)

R = 0% removal rate (due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation)

P = number of inhabitants in Sweden = $10 \cdot 10^6$

V (L/day) = volume of wastewater per capita and day = 200 (ECHA, 2008; Ref I).

D = factor of dilution of waste water by surface water flow = 10 (ECHA, 2008; Ref I).

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

Algae (Pseudokirchneriella subcapitata):

EC₅₀ 72 h (biomass): 79 000 µg/L

NOEC: 7200 µg/L

(Protocol: OECD 201)

(Ref II)

EC₅₀ 72 h (growth inhibition): 460 000 µg/L

NOEC: 23 000 µg/L

(Protocol: OECD 201)

(Ref II)

Crustacean (Daphnia magna):

EC₅₀ 48 h (immobilization): 191 000 µg/L

NOEC 48 h: 86 400 µg/L

(Protocol: FDA 4.08/OECD 202)

(Ref III)

EC₅₀ 21 days (reduction in reproduction): 15 600 µg/L

NOEC 21 days (reduction in reproduction): 10 400 µg/L

LOEC 21 days (reduction in reproduction): 23 300 µg/L

(Protocol: OECD 211)

(Ref IV)

Fish (Oncorhynchus mykiss):

LC₅₀ 96 h (mortality) > 290 000 µg/L

(Protocol: OECD 203)

(Ref IV)

Fish (Pimephales promelas):

NOEC 28 days (growth): 7040 µg/L

(Protocol: OECD 210)

(Ref VI)

Other ecotoxicity data:

PNEC = 704 µg/L, lowest EC₅₀/10 using results from the most sensitive chronic toxicity endpoint and an assessment factor of 10 (Long-term results from at least three species of the base set), to add a safety margin to the toxicity endpoint. The most sensitive species was *Pimephales promelas* for which the NOEC 28 days (growth) was 7040 µg/L.

Environmental Risk Classification (PEC/PNEC ratio)

PEC/PNEC= 0.184/704 = 0.000261, i.e. PEC/PNEC \leq 0.1 which justifies the phrase:
"Use of Irbesartan has been considered to result in insignificant environmental risk."

Degradation

Biotic degradation

Ready degradability:

Test results showed 22.5 % degradation in 28 days (FDA 3.11/OECD 301)
(Ref VII)

Simulation studies

DT50 in water:

DT50_{total system} = 8.7 (sediment 1) -12.5 (sediment 2) days. At the end of the study, there were 17.9% (sediment 1) and 23.9% (sediment 2) of parent compound remaining (in 100 days). Ambient extractions were carried out by shaking the sediment/solvent mixture at room temperature for 20 min. Reflux extraction was allowed to proceed for 4 h. The extract solution and sediment solids were separated by centrifugation. The non-extractable radioactivity in selected samples, where this was greater than 10 % of the applied radioactivity, was characterized using an acid/base fractionation procedure.
(Protocol: OECD 308)
(Ref VIII)

Abiotic degradation

Hydrolysis:

The half-life of Irbesartan was 40.1 days at pH 7, 25°C .
(Protocol: FDA 3.09/OECD111)
(Ref IX)

Photolysis:

Test showed a half-life of 6.41 h at pH 7.
(Protocol: FDA 3.10)
(Ref X)

Justification of chosen degradation phrase:

Irbesartan fails to pass the criteria for ready biodegradability. As DT50_{total system} < 32 days with still more than 15 % of the parent compounds remaining at the end of the study, the correct phrase is:
"Irbesartan is slowly degraded in the environment".

Bioaccumulation

Partition coefficient:

Log K_{ow} = 1.13 at pH 7 (OECD 107)
(Ref XI)

Justification of chosen bioaccumulation phrase:

Since log K_{ow} < 4 at pH 7, irbesartan has low potential for bioaccumulation.

Excretion (metabolism)

The substance is excreted almost exclusively as metabolites with only 2 % as unchanged.
(Ref XII)

Metabolites identified are (1) Tetrazole N2-beta-glucuronide conjugate of irbesartan, (2) monohydroxylated metabolite resulting from omega-1 oxidation of the butyl side chain, (3, 4) two different monohydroxylated

metabolites resulting from oxidation of the spirocyclopentane ring, (5) a diol resulting from omega-1 oxidation of the butyl side chain and oxidation of the spirocyclopentane ring, (6) a keto metabolite resulting from further oxidation of the omega-1 monohydroxy metabolite, (7) a keto-alcohol resulting from further oxidation of the omega-1 hydroxyl of the diol, and (8) a carboxylic acid metabolite resulting from oxidation of the terminal methyl group of the butyl side chain.

(Ref XIII)

The pharmacological activity of the metabolites is not known.

References

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