

Zofran®

M R F

Sandoz AS

Filmdragerad tablett 4 mg

(De filmdragerade tabletterna är gula, ovala och märkta GX ET3 (4 mg tabletterna) på ena sidan.)

Antiemetika.

Aktiv substans:

Ondansetron

ATC-kod:

A04AA01

Läkemedel från Sandoz AS omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Ondansetron

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

Nedbrytning: Ondansetron är potentiellt persistent.

Bioackumulering: Ondansetron har låg potential att bioackumuleras.

Detaljerad miljöinformation

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

$$\text{PEC } (\mu\text{g/L}) = (A \cdot 10^9 \cdot (100 - R)) / (365 \cdot P \cdot V \cdot D \cdot 100) = 1.37 \cdot 10^{-6} \cdot A \cdot (100 - R)$$
$$= 1.37 \cdot 10^{-6} \cdot 18.14 \cdot 100 = 0.025 \mu\text{g/L}$$

Where:

A = 18.14 kg ondansetron (total sold amount API in Sweden year 2021, data from IQVIA)

Total sold amount API in Sweden year 2021 is based on sum of sold ondansetronhydrokloriddihydrat (20.64 kg; molecular weight (MW): 365.9 g/mol ~ 16.55 kg free base) and ondansetron free base (1.5882 kg; MW: 293.4 g/mol), expressed as free base.

$$16.55 \text{ kg} + 1.5882 \text{ kg} = 18.14 \text{ kg ondansetron free base}$$

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 = $10 \cdot 10^6$

V (L/day) = volume of wastewater per capita and day = 200 (ECHA default) (ECHA 2008)

D = factor for dilution of waste water by surface water flow = 10 (ECHA default) (ECHA 2008)

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

Green Algae (Selenastrum capricornutum):

IC50 96 h (growth rate inhibition) > 3,100 µg/L (OECD 201)
(Reference 8)
NOEC = 620 µg/L

Water flea (Daphnia magna)

Acute toxicity

EC50 48 h (immobility) = 28,000 µg/L (OECD 202) (Reference 5)
NOEC = 14,000 µg/L

Water flea (Ceriodaphnia dubia)

Chronic toxicity

NOEC 7 d (reproduction) = 320 µg/L (USEPA 1002) (Reference 11)

Rainbow Trout (Oncorhynchus mykiss):

Acute toxicity

LC50 96 h (lethality) = 6,500 µg/L (OECD 203) (Reference 9)
NOEL = 2,600 µg/L

Fathead minnow (Pimephales promelas):

Chronic toxicity

No data

Other ecotoxicity data:

Microorganisms in activated sludge:

EC50 3 h (inhibition) > 1,000,000 µg/L @ 3 hrs (OECD 209)
(Reference 4)
NOEC = 100,000 µg/L

$PNEC = 320/100 = 3.20 \text{ µg/L}$

PNEC (µg/L) = lowest NOEC/100, where 100 is the assessment factor applied for two long-term NOECs when such results have not been generated from that showing the lowest L(E)C50 of the

short-term tests. The lowest NOEC for water flea (= 320 µg/L) has been used for this calculation since it is the most sensitive of the two tested species.

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.025 µg/L / 3.20 µg/L = 0.0008, i.e. PEC/PNEC ≤ 0.1 which justifies the phrase “Use of Ondansetron has been considered to result in insignificant environmental risk.”

Degradation

Biotic degradation

Ready degradability:

No data

Inherent degradability:

19% degradation in 28 days (OECD 302). (Reference 10)

Soil Metabolism:

20-99.9% degradation in 64 days (TAD 3.12) (Reference 7)

Abiotic degradation

Hydrolysis:

50% degradation (pH 7) > 1 year (TAD 3.09) (Reference 3)

Photolysis:

No data

Justification of chosen degradation phrase:

Ondansetron is not readily degradable nor inherently biodegradable. The phrase “Ondansetron is potentially persistent” is thus chosen.

Bioaccumulation

Partitioning coefficient:

Log Dow = 1.00 (TAD 3.02) (Reference 6)

Log Dow at pH 5 = 0.23

Log Dow at pH 7 = 1.00

Log Dow at pH 9 = 1.26

Justification of chosen bioaccumulation phrase:

Since log Dow < 4 at pH 7, the substance has low potential for bioaccumulation.

Excretion (metabolism)

Ondansetron is cleared from the systemic circulation predominantly by hepatic metabolism. Less than 5% of the absorbed dose is excreted unchanged in the urine. (Reference 2).

PBT/vPvB assessment

Ondansetron does not fulfil the criteria for PBT and/or vBvP.

All three properties, i.e. 'P', 'B' and 'T' are required in order to classify a compound as PBT (Reference 1). Ondansetron does not fulfil the criteria for PBT and/or vBvP based on log Dow < 4.

References

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6. Colwyn TC. GR38032X: Determination of Physico-Chemical Properties. Report No. 94/GLX171/1157. Pharmaco LSR Ltd, February 1995.
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10. Shaefer EC. Ondansetron hydrochloride: An Evaluation of Inherent Biodegradability Using the Zahn-Wellens Test. Report No. 374E-122A. Wildlife International Limited, March 2005.
11. Goodband TJ: Ondansetron hydrochloride: Daphnid, *Ceriodaphnia Dubia* Survival and Reproduction Test. Report No. 1127/01213. Safepharm Laboratories Limited, July 2007.