FASS

Diovan®

MRx EF

Novartis

Filmdragerad tablett 160 mg
(grå-orange, oval tablett, något konvex, brytskåra på ena sidan och märkt med DX på ena sidan av brytskåran och DX på andra sidan av brytskåran och NVR på den andra sidan av tabletten. Brytskåran är bara till för att underlätta nedsväljning.)

Angiotensin II-receptorblockerare

Aktiv substans:
Valsartan

ATC-kod:
C09CA03

Läkemedel från Novartis omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Valsartan

Miljörisk: Användning av valsartan har bedömts medföra försumbar risk för miljöpåverkan.
Nedbrytning: Valsartan bryts ned i miljön.
Bioackumulering: Valsartan 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) = $(A*10^{9}*(100-R))/(365*P*V*D*100) = 1.37*10^{-6} * A * (100 - R) = 1.37*10^{-6} * 1922.79 * 100 = 0.263$ µg/L

Where:

A = 1922.79 kg valsartan (sum of 1272.86 kg valsartan and 649.63 kg as valsartan proportion from amount of valsartan in 1429.04 kg sakubitril-valsartannatriumhydrat*) (total sold amount API in Sweden year 2021, data from IQVIA).

*The molecular weight of sacubritil-valsartan (Entresto®) is 1916 g/mol, and this contains two molecules of valsartan (435.5 g/mol x 2), so approx. 45.46% of the sacubritil-valsartan sodium hydrate corresponds to valsartan, which implies that the 1429.04 kg correspond to 649.63 kg valsartan.

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) (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 (Pseudokirchneriella subspicata) (OECD201) (NOTOX Project 490976):

EC50 72 h (growth rate) > 100.0 mg/L
NOEC = 100.0 mg/L
Crustacean (Daphnia magna):
Acute toxicity
EC50 48 h (immobilisation) > 100.0 mg/L (OECD202) (ECOTOXICOLOGY CIGY NO. 948128)
Chronic toxicity
NOEC 21 days (parental mortality and reproduction) = 5.6 mg/L (OECD 211) (NOTOX Study No. 464434)
Fish:
Acute toxicity (*Oncorhynchus mykiss*, rainbow trout)
LC50 96 h (mortality) > 100.0 mg/L (OECD203) (ECOTOXICOLOGY CIGY NO. 948130)
Chronic toxicity (*Pimephales promelas,* fathead minnow)
NOEC 30 days = 10.0 mg/L; no effect up to the highest concentration tested (OECD 210) (NOTOX Study No. 464445)
Other ecotoxicity data:
Bacterial respiration inhibition
EC_{50} 3 h > 750 mg/L
NOEC = 750 mg/L (activated sludge respiration inhibition) (OECD209) (NOTOX Project 490977)
Sediment-dwelling organisms (*Chironomus riparius*, non-biting midge)
NOEC 28 days = 400.0 mg/kg dry weight (OECD 218) (NOTOX Project 490978)
PNEC derivation:
PNEC = 560 µg/L
PNEC (µg/L) = lowest NOEC/10, where 10 is the assessment factor used if three chronic toxicity studies from three trophic levels are available. The NOEC for *Daphnia magna* reproduction has been used for this calculation.

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.263 µg/L / 560 µg/L = 0.00047, i.e. PEC/PNEC ≤ 0.1 which justifies the phrase "Use of valsartan has been considered to result in insignificant environmental risk."

Degradation

Biotic degradation

Ready degradability:

0 % degradation in 28 days, not readily biodegradable (92/69/EC (L383) C.4-C). (ECOTOXICOLOGY CIGY NO. 948127)

Simulation studies:

DT_{50} (total system) = 12.0 – 16.1 days

DT_{90} (total system) = 39.8 – 53.6 days (OECD 308, 191 days). (RCC Study No. B40590)

< 15 % parent substance remaining at the end of the study

45-50 % non-extractable residues at the end of the study (up to two times: acetonitrile:water (4:1, v/v), followed by soxhlet acetonitrile: water (4:1, v/v))

Justification of chosen degradation phrase:

According to the pass criteria for OECD308 studies, valsartan can be classified as ‘Valsartan is degraded in the environment' (DT_{50} for total system < 32 days)

Bioaccumulation

Partitioning coefficient:

Log Dow = 1.2 at pH 7 (OECD117)

Log P = 2.8 at pH 2.5 (NOTOX Project 490979)

Justification of chosen bioaccumulation phrase:

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

Excretion (metabolism)

Valsartan is primarily eliminated in feces (about 83% of dose) and urine (about 13% of dose), mainly as unchanged drug. (Diovan® (valsartan) Core Data Sheet, 2018)

PBT/vPvB assessment

Valsartan cannot be considered a potential PBT substance.

References

- ECHA 2008, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment. http://guidance.echa.europa.eu/docs/guidance_document/informa
- NOTOX Project 490976. Fresh water algal growth inhibition test with valsartan/DS 21. Final report: August 04, 2009.
- ECOTOXICOLOGY CIGY NO.948128.
- NOTOX Study No. 464434. *Daphnia magna* reproduction test with VAA489 VAL (semi-static). Final Report: Sept 26, 2006.
- ECOTOXICOLOGY CIGY NO. 948130.
- NOTOX Study No. 464445. Fish early-life stage toxicity test with VAA489 VAL (semi-static). Final Report: July 12, 2006.
- NOTOX Project 490977. Activated sludge respiration inhibition test with valsartan/DS 21. Final report: August 20, 2009.

- NOTOX Project 490978. Sediment-water Chironomid toxicity test using sediment spiked with valsartan/DS 21. Final report: October 01, 2009.
- ECOTOXICOLOGY CIGY NO. 948127. PBS 858 DS. Report on the test for ready biodegradability of PBS 858 DS in the carbondioxide evolution test. Final report: September 21, 1995.
- RCC Study No. B40590. 14C-VAH631 VAL DS. Route and rate of degradation in aerobic aquatic sediment systems. Final report: May 26, 2008.
- NOTOX Project 490979. Determination of the partition coefficient of valsartan/DS 21. Final report: July 01, 2009.
- DIOVAN® (valsartan). Core Data Sheet. Version 3.0. 10-Sep-2018.