FASS

Myfortic®

Novartis

Enterotablett 180 mg

(Ljusgrön, filmdragerad, rund tablett med fasad kant och präglad "C" på ena sidan.)

Immunsuppressivum

Aktiv substans:

Mykofenolsyra

ATC-kod:

L04AA06

Läkemedel från Novartis omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Natriummykofenolat

Miljörisk: Användning av natriummykofenolat har bedömts medföra medelhög risk för miljöpåverkan.
Nedbrytning: Natriummykofenolat är potentiellt persistent.
Bioackumulering: Natriummykofenolat 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) = $1.37*10^{-6}$ * 2880.9 * 100 = 0.395 µg/L
Where:
A = 2880.9 (Sum of 97 kg mycophenolate derived from 103.67 kg mycophenolate sodium and 2783.9 kg mycophenolate derived from 3767.31 kg mycophenolate mofetil) (total sold amount API in Sweden year 2021, data from IQVIA).
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

Algae (Selenastrum capricornutum) (OECD 201) (NOTOX Project 261686)*:*
EC50 96 h (growth rate) = 0.068 mg/L
NOEC = 0.01 mg/L

Cyanobacteria (Anabaena flos-aquae) (OECD 201) (Straub et al., 2019)
NOEC (growth rate) = 83.9 µg/L
ErC_{10} (growth rate) = 155.0 µg/L

Crustacean (Daphnia magna):
Acute toxicity
EC50 48 h (immobilisation) > 100.0 mg/L (OECD 202) (NOTOX Project 330424)

Chronic toxicity
NOEC 21 day (fecundity and reproduction) = 630 µg/L
EC_{10} 21 day (fecundity and reproduction) = 929 µg/L (OECD 211) (Straub et al., 2019)

Fish:
Acute toxicity (*Cyprinus carpio,* common carp)
LC50 96 h (mortality) > 100.0 mg/L (OECD 203) (NOTOX Project 330413)

Chronic toxicity
NOEC 34 days (length of surviving F1 fish) = 1.32 µg/L (zebrafish; *Danio rerio*) (OECD 229 / OECD 210) (Straub et al., 2019)

Other ecotoxicity data:
Bacterial respiration inhibition
EC_{50} 3 h = 2213.0 mg/L
EC_{10} 3h = 69.0 mg/L (activated sludge respiration inhibition) (OECD 209) (NOTOX Project 261697)
PNEC derivation:
PNEC = 132.0 ng/L
PNEC (µg/L) = lowest NOEC/10, where 10 is the assessment factor used if chronic toxicity studies from three trophic levels are available. The NOEC for fish has been used for this calculation.

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.395 µg/L / 132.0 ng/L = 395 ng/L / 132.0 ng/L = 2.99 ~ 3.0, i.e. PEC/PNEC ≥ 1 which justifies the phrase "Use of mycophenolate sodium has been considered to result in moderate environmental risk."

Degradation

Biotic degradation

Ready degradability:
2.0 – 5.0 % degradation in 28 days, not readily biodegradable (OECD301). (NOTOX Project 261708)

Justification of chosen degradation phrase:
Mycophenolate does not pass the criteria for ready biodegradation. Therefore, it can be classified as "Mycophenolate is potentially persistent."

Bioaccumulation

Partitioning coefficient:

Mycophenolic acid Log P: 1.6 (method unknown, no reference available) (Clarke's Analysis of Drugs and Poisons)

Justification of chosen bioaccumulation phrase:

The log P for mycophenolic acid remains below the trigger level of a bioaccumulative substance (< log P of 4). As mycophenolic acid is the active drug substance and the form that will be available in the environment, reference to the octanol-water partition coefficient of the free acid is made, rather than to the natrium salt or to mycophenolate mofetil. Based on the log P of mycophenolic acid, the following statement is chosen: "Mycophenolate sodium has low potential for bioaccumulation."

Excretion (metabolism)

Mycophenolate (MPA) is metabolised principally by glucuronyl transferase to from the phenolic glucuronide of MPA. Mycophenolic acid glucuronide (MPAG) does not manifest biologic activity. Although negligible amounts of MPA are present in the urine (< 1.0%), the majority of MPA is eliminated in the urine as MPAG. MPAG secreted in the bile is available for deconjugation by gut flora. The MPA resulting from this deconjugation may then be reabsorbed. (Novartis Core Data Sheet, 2013)

PBT/vPvB assessment

While Mycophenolate sodium fulfils the screening criteria for a persistent substance, no sufficient information for judging on the P criteria is available. Therefore, no conclusion on PBT potential is possible.

References

- ECHA 2008, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment. http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm
- NOTOX Project 261686. Fresh water algal growth inhibition test with ERL080/DS. Final report: 06.12.1999.
- JO Straub, R Oldenkamp, T Pfister and A Häner, 2019. Risk assessment for mycophenolic acid in European surface waters—Environmental Toxicology and Chemistry, 2019; 38: 2259–2278.
- NOTOX Project 330424. Acute toxicity in *Daphnia magna* with ERL080/DS (static). Final report: 26.08.2001.
- NOTOX Project 330413. 96-hour acute toxicity study in carp with ERL080/DS (static). Final report: 26.09.2001.
- NOTOX Project 261697. Activated sludge respiration inhibition test with ERL080/DS (contact time: 3 hours). Final report: 06.07.1999.
- NOTOX Project 261708. Determination of 'ready' biodegradability: carbon dioxide (CO2) evolution test (modified Sturm test) with ERL080/DS. Final report: 16.07.1999.
- Clarke's Analysis of Drugs and Poisons. 2007. Medicines Complete. https://www.medicinescomplete.com/mc/clarke/current/CLK1128.htm?q=mycophenolate&t=search&ss=t

Novartis Core Data Sheet, Myfortic®, Version 1.1, 30 October 2013.