

Myfortic[®]**M R F_f****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:

$$\text{PEC } (\mu\text{g/L}) = (A \cdot 10^9 \cdot (100 - R)) / (365 \cdot P \cdot V \cdot D \cdot 100) = 1.5 \cdot 10^{-6} \cdot A \cdot$$

$$(100 - R) = 1.5 \cdot 10^{-6} \cdot 2360.67 \text{ kg} \cdot 100$$

$$\text{PEC} = 0.3541 \mu\text{g/L}$$

Where:

A = 2360.67 (Sum of 108.5 kg mycophenolate derived from 115.95 kg mycophenolate sodium and 2252.17 kg mycophenolate derived from 3047.752 kg mycophenolate mofetil) (total sold amount API in Sweden year 2015, data from IMS Health).

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 = $9 \cdot 10^6$

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

Algae (Selenastrum capricornutum) (OECD 201) (NOTOX Project 261686):

EC50 96 h (growth rate) = 0.068 mg/L

NOEC = 0.01 mg/L

Crustacean (Daphnia magna):

Acute toxicity

EC₅₀ 48 h (immobilisation) > 100.0 mg/L (OECD 202) (NOTOX Project 330424)

Fish:

Acute toxicity (*Cyprinus carpio*, common carp)

LC₅₀ 96 h (mortality) > 100.0 mg/L (OECD 203) (NOTOX Project 330413)

Other ecotoxicity data:

Bacterial respiration inhibition

EC₅₀ 3 h = 2213.0 mg/L

EC₁₀ 3h = 69.0 mg/L (activated sludge respiration inhibition)
(OECD 209) (NOTOX Project 261697)

PNEC derivation:

PNEC = 68 ng/L

PNEC (µg/L) = lowest EC₅₀/1000, where 1000 is the assessment factor used if three acute toxicity studies from three trophic levels are available. The EC₅₀ for green algae has been used for this calculation.

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 354.1 ng/L / 68 ng/L = 5.21, i.e. PEC/PNEC ≤ 1.0 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 sodium 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 form 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/informa
- NOTOX Project 261686. Fresh water algal growth inhibition test with ERL080/DS. Final report: 06.12.1999.
- 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.f>

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