

Calcipotriol/Betamethasone Sandoz M R F

Sandoz AS

Salva 50 mikrogram/g + 0,5 mg/g
(Benvit.)

Övriga medel vid psoriasis för utvärtes bruk, Calcipotriol, kombinationer.

Aktiva substanser (i bokstavsordning):

Betametason

Calcipotriol (vattenfri)

ATC-kod:

D05AX52

Läkemedel från Sandoz AS omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Miljöinformationen för betametason är framtagen av företaget GlaxoSmithKline för Betnovat®, Betnovat® med chinofom, Betnovat® med neomycin

Miljörisk: Risk för miljöpåverkan av betametason kan inte uteslutas då det inte finns tillräckliga ekotoxikologiska data.

Nedbrytning: Betametason är potentiellt persistent.

Bioackumulering: Betametason har låg potential att bioackumuleras.

Detaljerad miljöinformation

Detailed background information

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

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

$$\text{PEC} = 0.064 \mu\text{g/L}$$

Where:

A = 465.29 kg (total sold amount API free base in Sweden year 2022, data from IQVIA). Total volume of Betametasone acetate = 0.23 = 0.21 Kg acetate free base. Total volume of Betametasone dipropionate = 473 = 368 Kg dipropionate free base. Total volume of Betametasone sodium phosphate = 25 = 19 Kg atrium phosphate free base. Total volume of Betametasone valerate = 69.57 = 57.29 Kg valerate free base.

R = 0% removal rate (conservatively, it has been assumed there is no 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 default) (Reference 1)

D = factor for dilution of waste water by surface water flow = 10 (ECHA default) (Reference 1)

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

Algae:

No data

Water flea (Daphnia magna):

Acute toxicity

EC₅₀ 48 h (immobility) = 1,900 µg/L (OECD 202) (Reference 3)

Water flea:

Chronic toxicity

No data

Fish:

Acute toxicity

No data

Chronic toxicity

No data

Other ecotoxicity data:

Microorganisms in activated sludge:

EC₅₀ 3 h (inhibition) > 1,000,000 µg/L (OECD 209) (Reference 4)

NOEC 3 h (inhibition) = 1,000,000

PNEC cannot be calculated because data is not available for all three (algae, crustacean and fish) of the toxicity endpoints.

Environmental risk classification (PEC/PNEC ratio)

Risk of environmental impact of betamethasone cannot be excluded, since there is not sufficient ecotoxicity data available.

Degradation

Biotic degradation

Ready degradability:

No data

Inherent degradability:

28% primary degradation in 28 days (OECD 302C) (Reference 5)

Abiotic degradation

Hydrolysis:

50% degradation (pH 7) = 6.5 days (TAD 3.09) (Reference 7)

Photolysis:

No data

Justification of chosen degradation phrase:

Betamethasone valerate is not readily degradable or inherently biodegradable but the parent API undergoes appreciable primary biodegradation. This substance is predicted to degrade via hydrolysis with a half-life is less than 40 days. However, relevant hydrolysis products have not been identified and characterised. The phrase “betamethasone valerate is potentially persistent” is thus chosen.

Bioaccumulation

Bioconcentration factor (BCF):

Partitioning coefficient:

$\log P_{ow} = 3.60$ (OECD 107). (Reference 6)

Justification of chosen bioaccumulation phrase:

Since $\log P_{ow} < 4$, the substance has low potential for bioaccumulation.

Excretion (metabolism)

Betamethasone: Topical mode of administration with up 14 % of betamethasone adsorbed systemically. This fraction is extensively metabolised in the liver. Only 4.8 % of the dose is recovered from urine, the remainder is eliminated as metabolites (Reference 2).

Please, also see Safety data sheets on
<http://www.msds-gsk.com/ExtMSDSlist.asp>.

References

1. ECHA, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment.
2. Petersen MC, Nation RL, McBride WG, et al: Pharmacokinetics of betamethasone in healthy adults after intravenous administration. *Eur J Clin Pharmacol* 1983; 25:643-650.
3. Sewell IG and McKenzie J. Betamethasone 17-Valerate: Acute Toxicity to *Daphnia magna*. Report No. 1127/304. Safeparm Laboratories Limited, May 2004.
4. Clarke N. Betamethasone 17-Valerate: Assessment of the Inhibitory Effect on the Respiration of Activated Sewage Sludge. Report No. 1127/306. Safeparm Laboratories Limited, May 2004.
5. Mead C and McKenzie J. Betamethasone 17-Valerate: Assessment of Inherent Biodegradability; Modified MITI (II) Test. Report No. 1127/305. Safeparm Laboratories Limited, July 2004.
6. Dołowy M, Pyka A. Evaluation of Lipophilic Properties of Betamethasone and Related Compounds. *Acta Pol Pharm.* 2015;72(4):671-681

7. Material Safety Data Sheet for Betnovate® GM Cream. SDS number 130046. GlaxoSmithKline plc, September 2007.