

Testogel®

M R_s F

Laboratoires Besins

Transdermal gel 50 mg

(Transparent eller lätt opaliserande, färglös gel)

Särskilt läkemedel

Androgener

Aktiv substans:

Testosteron

ATC-kod:

G03BA03

Läkemedel från Laboratoires Besins omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Miljöinformationen för testosteron är framtagen av företaget Bayer för Androgel®

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

Nedbrytning: Testosteron bryts ned långsamt i miljön.

Bioackumulering: Testosteron har hög potential att bioackumuleras.

Detaljerad miljöinformation

Testosterone, testosterone undecanoate

Testosterone enanthate is an ester of testosterone and a long fatty acid. The biological active moiety of this compound is testosterone. Therefore, this classification is based on testosterone.

Hazardous environmental properties: "Risk of environmental impact of testosterone cannot be excluded, since there is not sufficient ecotoxicity data".

Degradation: "Testosterone" is slowly degrading in the environment.

Bioaccumulation: "Testosterone" has a high potential for bioaccumulation.

Detailed background information

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

In order to normalize testosterone undecanoate on testosterone units, the sales volume was adjusted to the molecular weight of testosterone:

Testosterone	288.4 g/Mol	--
Testosterone undecanoate	456.7 g/Mol	0.63

PEC is calculated according to the following formula:

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

Where:

A = 150.84 kg testosterone equivalents as the total of 115.78 kg testosterone and 35.06 kg testosterone undecanoate (total sales data in Sweden in 2019 from IQVIA database).

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 (1))

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

Based on this formula and data the PEC was calculated as 0.023 µg/L.

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

Algae (Desmodesmus subspicatus):

NOEC 72 h (growth inhibition, growth rate) ≥ 1 mg/L (saturated solution) (OECD TG 201). (2)

Crustacean:

Acute toxicity (waterflea *Daphnia magna*):

EC50 48 h (immobilization) > 1.8 mg/L (saturated solution) (OECD TG 202). (3)

There is no data on chronic toxicity to crustaceans or fish.

Environmental risk classification (PEC/PNEC ratio)

Since no data on fish or any chronic aquatic hazard data are available, the risk of environmental impact of testosterone cannot be excluded, since there is not sufficient ecotoxicity data available.

Degradation

Biotic degradation

Ready degradability: not ready biodegradable

Testosterone enantate was studied for aerobic biodegradability in water in a manometric respiration test according to guideline OECD TG 301F (4). It was degraded to 60 % after 28 days. The degradation, however, proceeded slowly and did not fulfill the ready degradability criteria of OECD TG 301.

Abiotic degradation

Hydrolysis:

Testosterone enantate has a hydrolytical half-life of 218-374 days at pH 9 and 25°C and is stable at pH values ≤ 7 . (5)

Justification of chosen degradation phrase:

Since the biodegradation rate was 60% in a ready biodegradation test, but the stringent criteria for ready biodegradability was not met, and the substance is hydrolytically stable, the phrase "Testosterone is slowly degraded in the environment" is justified.

Bioaccumulation

Partitioning coefficient:

Log K_{OW} of 7 at pH 7 and 25°C for testosterone enantate (Shake flask method, OECD TG 117). (6)

Justification of chosen bioaccumulation phrase:

As the log K_{OW} is 7, the phrase "testosterone has a high potential for bioaccumulation" is justified.

Excretion (metabolism)

Testosterone is only to a small extent excreted unchanged (7). Conjugates such as glucuronides and sulphates as well as androsterone and etiocholanolone were identified (8).

PBT/vPvB assessment

A conclusion on PBT properties is not possible as data on chronic toxicity is missing. The substance is unlikely to be vPvB as a high percentage of biodegradation (failing the criteria for ready biodegradation) was observed.

References

- (1) ECHA, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment.
- (2) Growth inhibition test of testosterone enantate (ZK5137) on the green algae *Desmodesmus subspicatus*. Experimental Toxicology, Schering AG, study no. TXST20020330, report no. A18033 (2006)
- (3) Acute immobilization of testosterone enantate (ZK5137) with *Daphnia magna*. Experimental Toxicology, Schering AG, study no. TXST20020331, report no. A18429 (2005)
- (4) Study on the biodegradability of testosterone enantate (ZK5137) in the manometric respiration test. Experimental Toxicology, Schering AG, study no. TX20020321, report no. A14328 (2002)
- (5) Testosterone enantate/ ZK00005137/Report on physicochemical properties/Estimation of hydrolytic stability on basis of hydrolytic behavior of structurally similar compounds. Analytical Development Physical Chemistry, Schering AG, study no. 1274, report no. A 09814 (1999)
- (6) Bayer AG Safety data sheet according to Regulation (EC) No. 1907/2006, No. 122000004039 Testosterone Enanthate Version 10.0 Revision Date 01.02.2016
- (7) Melmed S, Polonsky KS, Larsen PR, Kronenberg HM. Williams Textbook of Endocrinology. Elsevier Health Sciences. pp. 711 (2015)
- (8) Cumming DC, Wall SR . Non-sex hormone-binding globulin-bound testosterone as a marker for hyperandrogenism. The Journal of Clinical Endocrinology and Metabolism. 61 (5): 873-6 (1985)