

## Testavan

### Ferring

Transdermal gel 20 mg/g  
(Homogen, genomskinlig till lätt opaliserande gel.)

*Särskild receptblankett krävs*

Androgener

### Aktiv substans:

Testosteron

### ATC-kod:

G03BA03

Läkemedel från Ferring omfattas av Läkemedelsförsäkringen.

## Miljöpåverkan

Miljöinformationen för testosteron är framtagen av företaget Bayer för Androgel®, Nebido®, Testogel®

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 including testosterone enantate

#### Environmental Risk Classification

#### Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

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

$$PEC = 0.0197 \mu\text{g/L}$$

Where:

**A = 102.8976 kg testosterone + 45.9878 kg testosterone undecanoate = 131.86 kg** (normalized on testosterone) (total sold amount API in Sweden year 2016, data from QuintilesIMS).

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 waterflow = 10 (ECHA default (1))

## **Predicted No Effect Concentration (PNEC)**

### **Ecotoxicological studies**

*Algae (Desmodesmus subspicatus):*

NOEC /72 h (growth inhibition, growth rate)  $\geq$  saturated solution [ca. 1 mg/L] (guideline OECD 201) (2)

*Crustacean (waterflea Daphnia magna):*

Acute toxicity

EC50 /48 h (immobilization)  $>$  saturated solution [ca. 1 mg/L] (guideline OECD 202) (3)

## **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 readily biodegradable

Testosterone enantate was studied for aerobic biodegradability in water in a manometric respiration test according to guideline OECD 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 301.

### **Abiotic degradation**

*Hydrolysis:*

Testosterone enantate has a hydrolytical half-life at pH 9 and 25°C of 218 to 374 days, and is stable at pH values  $\leq 7$  (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  $P_{OW}$  7 at pH 7 and 25°C for testosterone enantate (Shake flask method, OECD 117) (6)

*Justification of chosen bioaccumulation phrase:*

Since Log  $P_{OW}$  (at pH 7) 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 etiochonalonone were identified (8).

## **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)