

## Cozaar<sup>®</sup>

M R EF

### MSD

Filmdragerad tablett 50 mg

(vit, oval, längd 10,3 mm, bredd 5,6 mm, ena sidan märkt 952, den andra sidan skårad)

Angiotensin II-antagonist

### Aktiv substans:

Losartan

### ATC-kod:

C09CA01

Läkemedel från MSD omfattas av Läkemedelsförsäkringen.

## Miljöpåverkan

### Losartan

Miljörisk: Användning av losartan har bedömts medföra försumbar risk för miljöpåverkan.

Nedbrytning: Losartan är potentiellt persistent.

Bioackumulering: Losartan har låg potential att bioackumuleras.

## Detaljerad miljöinformation

## Environmental Risk Classification

### Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

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

$$\text{PEC} = 1.2 \mu\text{g/L}$$

Where:

A = 8161 kg (total sold amount API in Sweden year 2015, data from IMS Health).

R = 0 % removal rate (worst case assumption)

P = number of inhabitants in Sweden =  $9 \cdot 10^6$

V (L/day) = volume of wastewater per capita and day = 200 (ECHA default) (Ref. I)

D = factor for dilution of waste water by surface water flow = 10 (ECHA default) (Ref. I)

### Predicted No Effect Concentration (PNEC)

#### Ecotoxicological studies

*Green Algae (Selenastrum capricornutum)* (FDA 4.01) (Ref. II):

NOEC 10 day (cell growth) = 143 mg/L

*Blue Green Algae (Microcystis aeruginosa)* (FDA 4.01) (Ref. III):

NOEC 10 day (cell growth) = 556 mg/L

*Crustacean, water flea (Daphnia magna):*

Acute toxicity

LC<sub>50</sub> 48 h (mortality) = 331 mg/L (OECD 202) (Ref.IV)

NOEC = 80 mg/L

Chronic toxicity

NOEC 21 day (survival, reproduction, growth) = 100 mg/L (OECD 211) (Ref V)

No effects noted up to the highest concentration tested

*Fish, fathead minnow (Pimephales promelas):*

Acute toxicity

LC<sub>50</sub> 48 h (mortality) > 1000 mg/L (U.S. EPA "Methods for Measuring the Acute Toxicity of Effluents to Fresh Water and Marine Organisms", 1985) (Ref.IV)

NOEC = 100 mg/L

Chronic toxicity

NOEC 32-day (survival, hatching, growth) = 10 mg/L (OECD 210) (Ref VI)

No effects noted up to the highest concentration tested

*Fish, rainbow trout (Oncorhynchus mykiss):*

Acute toxicity

LC<sub>50</sub> 96 h (mortality) > 929 mg/L (FDA 4.11) (Ref.VII)

NOEC = 929 mg/L

PNEC = 1000 µg/L (10000 µg/L/ 10 based on the most sensitive chronic NOEC for the fish with an assessment factor (AF) of 10)

## **Environmental risk classification (PEC/PNEC ratio)**

PEC/PNEC = 1.2/1000 = 0.001, i.e. PEC/PNEC  $\leq$  .1 which justifies the phrase "Use of losartan has been considered to result in insignificant environmental risk."

## **Degradation**

### **Biotic degradation**

Bacteria > 90% of initial concentration remaining

Algal = 71% of initial concentration remaining after 28 days (FDA 3.11). (Ref VIII)

### **Abiotic degradation**

#### *Hydrolysis:*

Hydrolytically stable between pH 5-9 (FDA 3.09). (Ref. IX)

#### *Photolysis:*

Susceptible to aqueous photolysis and rapidly degrades under clear sky conditions

Half-Life<sub>max</sub> < 18 hours (pH 9) over wavelength interval 290-800

nm

(FDA 3.10). (Ref. X)

#### *Justification of chosen degradation phrase:*

Losartan has been found to degrade under natural light conditions however no data are available on metabolites. Therefore the phrase "Losartan is potentially persistent" was thus chosen.

## **Bioaccumulation**

#### *Partitioning coefficient:*

$\text{Log } K_{ow} = 1.2$  (OECD 107). (Ref.XI)

*Justification of chosen bioaccumulation phrase:*

Since  $\text{log } K_{ow} < 4$  at pH 7, the substance has low potential for bioaccumulation

## References

- I. ECHA, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment. [http://guidance.echa.europa.eu/docs/guidance\\_document/informa](http://guidance.echa.europa.eu/docs/guidance_document/informa)
- II. Toxikon Environmental Sciences, 1993. "Losartan (MK-0954): Toxicity to the Freshwater Green Alga, *Selenastrum capricornutum*, Under Static Test Conditions," Study No., J9209001f, TOX, Jupiter, FL, USA, 16 June 1993.
- III. Toxikon Environmental Sciences, 1993. "Losartan (MK-0954): Toxicity to the Blue-Green Alga, *Microcystis aeruginosa*, Under Static Test Conditions," Study No., J9209001g, TOX, Jupiter, FL, USA, 16 June 1993.
- IV. Merck, 1995. "Environmental Quality Criteria Monograph for Losartan Potassium", Merck & Co., Inc. Whitehouse Station, NJ, USA, 24 November 1995.
- V. Smithers Visicent, 2013. "Losartan - Full Life-Cycle Toxicity Test with Water Fleas, *Daphnia magna*, Under Static Renewal Conditions Following OECD Guideline #211" Smithers Visicent Study Number 359.6707" Wareham, MA, USA, 18 June 2013.
- VI. Smithers Visicent, 2013. "Losartan - Early Life-Stage Toxicity Test with Fathead Minnow, *Pimephales promelas*, Following OECD Guideline #210" Smithers Visicent Study Number 359.6706" Wareham, MA, USA, 10 June 2013.

- VII.** Toxikon Environmental Sciences, 1993. "Losartan (MK-0954): Acute Toxicity to Rainbow Trout, *Oncorhynchus mykss*, Under Static Test Conditions," Study No., J9209001i, TOX, Jupiter, FL, USA, 28 May 1993.
- VIII.** Toxikon Environmental Sciences, 1993. "Losartan (MK-0954): Biodegradation Inoculum Source Screening and Aerobic Biodegradation in Water," Study No., J9209001d, TOX, Jupiter, FL, USA, 06 August 1993.
- IX.** Toxikon Environmental Sciences, 1993. "Losartan (MK-0954): Determination of the Rate of Hydrolysis as a Function of pH," Study No., J9209001b, TOX, Jupiter, FL, USA, 02 March 1993.
- X.** Toxikon Environmental Sciences, 1993. "Losartan (MK-0954): Determination of Aqueous Photolysis," Study No., J9209001c, TOX, Jupiter, FL, USA, 02 July 1993.
- XI.** Merck & Co., Inc., 1995 "New Drug Application for Tablets Losartan Potassium, Environmental Assessment, Feb 1 1995"