FASS

# CELSENTRI®

MRx EF

**GlaxoSmithKline**

Filmdragerad tablett 150 mg

(Blå, bikonvexa, ovala, filmdragerade tabletter, ungefär 8,56 mm x 15,5 mm stora och präglade med ”MVC 150”.)

Virushämmande medel, direkt verkande; övriga antivirala medel

**Aktiv substans:**

Maravirok

**ATC-kod:**

J05AX09

Läkemedel från GlaxoSmithKline omfattas av Läkemedelsförsäkringen.

## Miljöpåverkan

### Maravirok

Miljörisk: Användning av maravirok har bedömts medföra försumbar risk för miljöpåverkan.
Nedbrytning: Maravirok är potentiellt persistent.
Bioackumulering: Maravirok 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:

PEC (µg/L) = $(A*10^{9}*(100-R)/(365*P*V*D*100) = 1.37*10^{-6}*A(100-R)$

PEC = 0.000016 µg/L

Where:
A = 0.12 kg (total sold amount API in Sweden year 2020, data from IQVIA).

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 = $10*10^6$

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

*Green Algae (Pseudokirchnereilla subcapita):*
IC50 72h (growth) > 115,000 µg/L (OECD 201) (Reference 3)

*Water flea (Daphnia magna):*
*Acute toxicity*
EC50 48 h (immobility) > 69,000 µg/L (OECD 202) (Reference 3)

*Water flea (Ceriodaphnia dubia):*
*Chronic toxicity*
LOEC 7 days (reproduction) > 92,000 µg/L (EPA 1002) (Reference 3)
NOEC = 92,000 µg/L

*Rainbow Trout (Juvenilee Ocorhynchus mykiss):*
*Acute toxicity*
LC50 96 h (lethality) > 73,000 µg/L (OECD 203) (Reference 3)

*Other ecotoxicity data:*
*Microorganisms in activated sludge*
EC50 3 hours (Inhibition) > 1,000,000 µg/L (OECD 209) (Reference 3)

PNEC = 92,000/100 = 920 µg/L

*PNEC (µg/L) = lowest NOEC/100, where 100 is the assessment factor applied for one long-term NOEC. NOEC for water flea (= 92,000 ug/L) has been used for this calculation since it is the most sensitive of the three tested species.*

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.000016/920 = $2.19x\ 10^{-9}$, i.e. PEC/PNEC ≤ 1 which justifies the phrase “Use of maraviroc has been considered to result in insignificant environmental risk.”

Degradation

Biotic degradation

*Ready degradability:*

1.70-2.60% degradation in 100 days (OECD 301B) (Reference 3)

*Inherent degradability:*
No Data

### Abiotic degradation

*Hydrolysis:*
No Data

*Photolysis:*
No Data

*Justification of chosen degradation phrase:*
Maraviroc is not readily biodegradable nor inherently biodegradable. The phrase “Maraviroc is potentially persistent” is thus chosen.

### Bioaccumulation

*Partitioning coefficient:*
Log $Dow_{calc}$ = 1.28 at pH 7 (Reference 4)

Log $Dow_{calc}$ at pH 5 = 0.17

Log $Dow_{calc}$ at pH 7 = 1.28

Log $Dow_{calc}$ at pH 9 = 3.10

*Justification of chosen bioaccumulation phrase:*
Since log Pow < 4, the substance has low potential for bioaccumulation.

### Excretion (metabolism)

Studies in humans and in vitro studies using human liver microsomes and expressed enzymes have demonstrated that maraviroc is principally metabolized by the cytochrome P450 system to metabolites that are essentially inactive against HIV-1. In vitro studies indicate that CYP3A4 is the major enzyme responsible for maraviroc metabolism. In vitro studies also indicate that polymorphic enzymes CYP2C9, CYP2D6 and CYP2C19 do not contribute significantly to the metabolism of maraviroc. Maraviroc is the major circulating component (approximately 42% radioactivity) following a single oral dose of 300 mg. The most significant circulating metabolite in humans is a secondary amine (approximately 22% radioactivity) formed by N-dealkylation. This polar metabolite has no significant pharmacological activity. Other metabolites are products of mono-oxidation and are only minor components of plasma radioactivity.

A mass balance/excretion study was conducted using a single 300 mg dose of 14C-labeled maraviroc. Approximately 20% of the radiolabel was recovered in the urine and 76% was recovered in the faeces over 168 hours. Maraviroc was the major component present in urine (mean of 8% dose) and faeces (mean of 25% dose). The remainder was excreted as metabolites. After intravenous administration (30 mg), the half-life of maraviroc was 13.2 h, 22% of the dose was excreted unchanged in the urine and the values of total clearance and renal clearance were 44.0 L/h and 10.17 L/h respectively (Reference 2).

### PBT/vPvB assessment

Maraviroc does not fulfil the criteria for PBT and/or vBvP.

All three properties, i.e. ‘P’, ‘B’ and ‘T’ are required in order to classify a compound as PBT (Reference 1). Maraviroc does not fulfil the criteria for PBT and/or vBvP based on a log Dow < 4.

**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. Pharmacokinetic properties: Metabolism and Elimination. Summary of Product Characteristics Celsentri (Maraviroc) 300mg Film Coated Tablets. ViiV Healthcare UK Ltd., May 2013.

3. MSDS PZ00608. Maraviroc Film Coated Tablets. Pfizer Ltd., September 2009.

4. Chemaxon /LogD (calculated). July 2013. Instant J Chem, ChemAxon Ltd.