

## Haldol®

M R F

**Janssen**

Tablett 1 mg

(vit, rund, bikonvex tablett, brytskåra på ena sidan och med inskriptionen "JANSSEN" på den andra sidan)

Neuroleptikum med antiemetisk effekt

**Aktiv substans:**

Haloperidol

**ATC-kod:**

N05AD01

Läkemedel från Janssen omfattas av Läkemedelsförsäkringen.

## Miljöpåverkan

### Haloperidol

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

Nedbrytning: Det kan inte uteslutas att haloperidol är persistent, då data saknas.

Bioackumulering: Haloperidol har hög potential att bioackumuleras.

# Detaljerad miljöinformation

## 1. PREDICTED ENVIRONMENTAL CONCENTRATION (PEC):

The Predicted Environmental Concentration is calculated according to the following formula:

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

Where:

A (kg/year)	=	11.2996502 kg (total sold amount API in the most recent sales data for Sweden (2016) was distributed by QuintilesIMS in summer 2017)
R (%)	=	removal rate (due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation)
	=	0% (worst-case scenario: no removal)
P	=	number of inhabitants in Sweden ( $9 \times 10^6$ )
V (L/day)	=	

	=	volume of waste water per capita and day
	=	200 (ECHA default) [6]
D	=	factor for dilution of waste water by surface water flow
	=	10 (ECHA default) [6]
PEC (µg/L)	=	0.001719886 µg/L

## 2. PREDICTED NO EFFECT CONCENTRATION (PNEC)

### 2.1.1. Ecotoxicological studies

#### 2.1.1.1. Algae

Algal growth inhibition test with the green alga (*Pseudokirchneriella subcapitata*) (OECD 201) [1]:

$E_b C_{50} 72 \text{ h} = 0.73 \text{ mg/L}$

$NOEC_b = 2.3 \text{ mg/L}$  (see detailed information in footnote "a" of the table below)

$E_r C_{50} 72 \text{ h} = 1.7 \text{ mg/L}$

$NOEC_r 72 \text{ h} = 0.37 \text{ mg/L}$

Biological Parameter	Based on Mean Measured Concentrations (mg a.i./L)			
	EC10 (95% Confidence Limits)	EC20 (95% Confidence Limits)	EC50 (95% Confidence Limits)	NOEC
0 - 72-Hour Average Growth Rate	0.55 (0.53 - 0.57)	0.75 (0.73 - 0.77)	1.7 (1.6-1.7)	0.37
0- to 72-Hour Yield	0.42 (0.38 - 0.44)	0.50 (0.47 - 0.52)	0.73 (0.71 - 0.74)	2.3 <sup>a</sup>

<sup>a</sup> Based on Kruskal-Wallis' Test, the NOEC was determined to be 2.3 mg a.i./L. A more reasonable estimate of the NOEC is the  $E_r C_{10}$  or  $E_r C_{20}$  (0.42 or 0.50, respectively) as suggested by the OECD Guideline (2006).

## 2.1.2 Crustacean

### Acute

Acute Toxicity to water fleas *Daphnia magna*(OECD 202) [2]

EC<sub>50</sub> 48 h > 2.91 mg/L

NOEC = 0.98 mg/L (immobility)

### Chronic

Not available

## 2.1.3 Fish

### Acute

Zebra fish (*Brachydanio rerio*):

LC<sub>50</sub> 96 h = 1.4 mg/L (OECD 203) [3]

NOEC = 0.56 mg/L (mortality)

### Chronic

Not available

## 2.1.4. Other ecotoxicity data

Activated sludge respiration inhibition test (OECD 209) [4]

EC<sub>50</sub> 3h > 1000 mg/L

NOEC 3h ≥ 1000 mg/L

## 2.2. Calculation of Predicted No Effect Concentration (PNEC)

PNEC (µg/l) = lowest LC<sub>50</sub>/1000, where 1000 is the assessment factor used.

The LC<sub>50</sub> for the Zebra fish (*Brachydanio rerio*) 1.4 mg/L has been used for this calculation since it is the most sensitive of the three tested species. As for the algae species, the growth rate endpoint has been chosen in favour of that of the algae biomass in the

determination of the PNEC. According to the OECD 201 guideline, preference should be given to the growth rate endpoint.

$$\text{PNEC} = 1.4 \text{ mg/L} / 1000 = 1.4 \text{ } \mu\text{g/L}$$

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

$$\text{PEC/PNEC} = 0.001719886/1.4 = 0.00122849 \text{ i.e. } \text{PEC/PNEC} \leq 0.1$$

#### **Conclusion for environmental risk:**

Use of Haloperidol has been considered to result in insignificant environmental risk.

## **3. DEGRADATION**

### **3.1. Biotic degradation**

#### **3.1.1. Ready biodegradation**

No data available.

The potential for persistence cannot be excluded due to lack of data.

## **4. BIOACCUMULATION**

### **4.1. Partition coefficient octanol/water**

The partition coefficient octanol/water was determined using the shaking flask method. [5]

$$\log D_{ow} = 4.76 \text{ (pH} = 3\text{)}$$

As  $\log K_{ow} \geq 4$ , Haloperidol has the potential to bioaccumulate in aquatic organisms.

#### **Conclusion for bioaccumulation:**

Haloperidol has high potential for bioaccumulation

## 5. REFERENCES

1. Softcheck K., Haloperidol - Acute Toxicity to the Freshwater Green Alga *Pseudokirchneriella subcapitata*. Springborn Smithers Study No. 13674.6157. Janssen Study No. RMD893; March 1, 2007.
2. Schmidt T., Acute Toxicity of Haloperidol (R001625) to *Daphnia Magna* in a 48-Hour Immobilization Test. RCC Study No. 857835, Janssen Study No. RMD626; January 26, 2005.
3. Sayers L., Haloperidol - Acute Toxicity to Zebra Fish (*Brachydanio rerio*), Under Static-Renewal Conditions. Springborn Smithers Study No. 13674.6158. Sponsor Protocol/Project No. RMD895; March 12, 2007.
4. McLaughlin S., Haloperidol - Activated Sludge Respiration Inhibition. Springborn Smithers Study No. 13674.6159. Janssen No. RMD896; March 8, 2007.
5. Jenkins K., Haloperidol - Determination of the  $K_{oc}$  Coefficient Following OECD Guideline 121. Springborn Smithers Study No. 13674.6156. Janssen N. RMD892. April 9, 2007.
6. 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)