

Concerta[®]



Janssen

Depottablett 18 mg

(kapselformad, gul, med svart tryck, alza 18, på ena sidan, Ø 5,3 mm längd 12 mm)



Narkotikaklass: II - Narkotika med medicinsk användning

Särskilt läkemedel

Medel vid ADHD

Aktiv substans:

Metylfenidat

ATC-kod:

N06BA04

Läkemedel från Janssen omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Metylfenidat

Miljörisk: Användning av metylfenidat har bedömts medföra medelhög risk för miljöpåverkan.

Nedbrytning: Metylfenidat bryts ned i miljön.

Bioackumulering: Metylfenidat har låg potential att bioackumuleras.

Detaljerad miljöinformation

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

$$\text{PEC } (\mu\text{g/L}) = (A \cdot 10^9 \cdot (100 - R)) / (365 \cdot P \cdot V \cdot D \cdot 100) = 1.37 \cdot 10^{-6} \cdot A \cdot (100 - R)$$

$$\text{PEC} = 0.14772309316889 \mu\text{g/L}$$

Where:

A = total actual API sales in Sweden for the most recent year 1078.27075 kg (total sold amount API in the most recent sales data for Sweden (2022) was distributed by IQVIA in 2023)

R = 0

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

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

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

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

Algae (Scenedesmus subspicatus) (guideline e.g. OECD 201):

Algal growth inhibition test [Reference II]:

EyC₅₀ 72 h (yield) = 6 mg/L

NOEC_y (yield) = 0.77 mg/L

NOEC_r (growth) = 0.77 mg/L

Crustacean (Daphnia magna) (water-flea):

Acute toxicity

Immobilization test (guideline e.g. OECD 202) (Reference III):

EC50 (48h) = 42 mg/l

NOEC (48h) = 5.4 mg/l

Chronic toxicity

Effect on survival and Reproduction (guideline e.g. OECD 211) [Reference IV]:

NOEC 21 days = 5.2 mg/L (Reproduction and survival)

LOEC 21 days = 17 mg/L (Reproduction and survival)

Fish:

Acute toxicity

Acute toxicity to zebra fish (*Brachydanio rerio*) (guideline e.g. OECD 203) (Reference V):

LC50 (96 h): > 100 mg/l

NOEC (96 h): >= 100 mg/l

Chronic toxicity

Fish early life stage test with zebra fish (*Brachydanio rerio*) (guideline e.g. OECD 210) (Reference VI):

NOEC 35 days = 3.3 mg/L (weight)

LOEC 35 days = 11 mg/L (weight)

Other ecotoxicity data:

Activated sludge respiration inhibition test (OECD 209) [Reference VII]

EC₅₀ (3h): > 1000 mg/L

NOEC (3h): 326 mg/L

PNEC (µg/l) = lowest NOEC/10, where 10 is the assessment factor used. NOEC for *Scenedesmus subspicatus* of 0.77 mg/L has been used for this calculation since it is the most sensitive of the three tested species.

PNEC = 0.77 mg/L/10 = 0.077 µg/L

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.14772309316889 /0.077 = 1.918481729

Conclusion for environmental risk:

The calculated PEC/PNEC ratio is between 1 and 10.

Use of Methylphenidate has been considered to result in moderate environmental risk.

Degradation

Biotic degradation

Ready biodegradation

Methylphenidate HCl was investigated for its ready biodegradation an aerobic aqueous medium with microbial activity introduced by inoculation with activated sludge according to OECD 301F [Reference VIII]:

Biodegradation: 77 % and 75 %

Toxicity: No inhibition of microbial activity.

Conclusion: Methylphenidate Hydrochloride was readily biodegradable under the conditions of the Manometric Respirometry Test

Simulation studies:

Aerobic degradation in aquatic sediment systems:

Methylphenidate Hydrochloride was investigated for its aerobic degradation in two aquatic systems (river and pond), according to OECD 308 [Reference IX].

The rates of dissipation (DT50, DT90) of ¹⁴C-Methylphenidate HCl from the total system were calculated using first order kinetics and the Origin calculation software. All calculated DT50 and DT90 values are summarized in the following table:

| System | ¹⁴ C-Methylphenidate (Total system) | |
|--------|---|-----------------------------|
| | DT ₅₀ [hours] | DT ₉₀ [hours] |
| River | 8.3 | 27.5 |
| Pond | 7.0 | 23.2 |

Methylphenidate HCl dissipated rapidly from the total system mainly due to hydrolysis with DT50 values of 8.3 hours for the river and 7.0 hours for the pond system, respectively.

In aquatic systems, Methylphenidate HCl hydrolysed rapidly to Ritalinic acid which was further degraded and mineralised after adsorption to the sediment.

Anaerobic degradation in aquatic sediment systems:

Methylphenidate Hydrochloride was investigated for its aerobic degradation in an aquatic system (pond), according to OECD 308 [Reference X].

The following dissipation half-lives and DT90 values were calculated for the parent compound ¹⁴C-Methylphenidate HCl. The Origin software was used for calculations.

| System | ¹⁴ C-Methylphenidate (Total system)* | |
|--------|--|------------------|
| | DT ₅₀ | DT ₉₀ |
| | [hours] | [hours] |
| Pond | 8.5 | 28.4 |

*: Calculated by applying first-order kinetics.

Methylphenidate HCl dissipated rapidly from the total system mainly due to hydrolysis with a DT50 value of 8.5 hours for the anaerobic pond system.

In anaerobic aquatic systems, Methylphenidate HCl hydrolysed rapidly to Ritalinic acid. The majority of the Ritalinic acid remained in the water phase whereas a part dissipated from the water phase by adsorption to the sediment. Ritalinic acid was degraded and mineralised slowly under anaerobic conditions.

Conclusion for degradation: Methylphenidate HCl is degraded in the environment.

Abiotic degradation

Hydrolysis: -

Photolysis: -

Bioaccumulation

Partition coefficient octanol/water:

The partition coefficient octanol/water of Methylphenidate HCl was determined with modeling software (ACD/I-Lab 2.0) [Reference XI]

pH 7

log D = 0.32

method: modeling software ACD/I-Lab 2.0

Bioconcentration factor (BCF):

No data available.

Conclusion for bioaccumulation: Methylphenidate HCl has low potential for bioaccumulation.

Excretion (metabolism)

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PBT/vPvB assessment

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References

- I. ECHA, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment.
http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm
- II. Bättscher R. Methylphenidate HCl: Toxicity to *Scenedesmus subspicatus* in a 72-hour algal growth inhibition test. OECD 201. RCC Ltd Study Number A46945, Janssen Study Number RMD736. May 2007.
- III. Bättscher R. Methylphenidate HCl: Acute toxicity to *Daphnia magna* in a 48-hour immobilization test. OECD 202. RCC Ltd Study Number A46967, Janssen Study Number RMD737. May 2007.
- IV. Höger S. Methylphenidate HCl: Effect on survival and reproduction of *Daphnia magna* in a Semi-Static Test over three weeks. OECD 211. RCC Ltd Study Number B79165, Janssen Study Number RMD1014. September 2008.
- V. Peither A. Methylphenidate HCl: Acute toxicity to zebra fish (*Brachydanio rerio*) in a 96-hour semi-static test. OECD 203. RCC Ltd Study Number A46980, Janssen Study Number RMD738. May 2007.
- VI. Peither A. Methylphenidate HCl: Toxic effects to zebra fish (*Brachydanio rerio*) in an Early-Life Stage toxicity test. OECD 210. RCC Ltd Study Number B79187, Janssen Study Number RMD1015. April 2009.
- VII. Seyfried B. Methylphenidate HCl: Toxicity to activated sludge in a respiration inhibition test. OECD 203. RCC Ltd Study Number A47002, Janssen Study Number RMD739. May 2007.
- VIII. Timmer N. Determination of 'Ready' Biodegradability: Manometric Respirometry Test of Methylphenidate HC USP/EP. OECD 203. Charles River Laboratories Den Bosch BV, Facility Study Number 20298426, Janssen Study Number RMD1338. December 2021.
- IX. Fahrbach M. 14C-Methylphenidate Hydrochloride: route and rate of degradation in aerobic aquatic sediment systems. Harlan Laboratories Study B79143, Janssen Reference Number RMD1012, June 2009.
- X. Fahrbach M. 14C-Methylphenidate Hydrochloride: route and rate of degradation in an anaerobic aquatic sediment system. Harlan Laboratories Study B79154, Janssen Reference Number RMD1013, June 2009.
- XI. Methylphenidate HCl, Determination of Partition Coefficient (n-Octanol/Water), Harlan Laboratories Study C15776, Janssen Reference Number RMD1028, May 2015.