FASS

Cerazette®

MSD

Filmdragerad tablett 75 mikrog

(Vita, runda, 5 mm, märkta KV 2 på ena sidan och ORGANON* på den andra)

Antikonceptionella medel, Gestagener.

Aktiv substans:

Desogestrel

ATC-kod:

G03AC09

Läkemedel från MSD omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Desogestrel

Miljörisk: Användning av desogestrel har bedömts medföra medelhög risk för miljöpåverkan.
Nedbrytning: Desogestrel bryts ned långsamt i miljön.
Bioackumulering: Desogestrel har låg potential att bioackumuleras.

Detaljerad miljöinformation

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

PEC (µg/L) = $(A*10^{9}*(100-R))/(365*P*V*D*100) = 1.5*10^{-6}*A(100-R)$

PEC = 0.0005 ug/L

Where:
A = 3.6 kg (total sold amount API in Sweden year 2016, data from QuintilesIMS).
R = 0 % removal rate (worst case assumption)

P = number of inhabitants in Sweden = 9 *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)

Desogestrel is a prodrug progestogen and is rapidly metabolized to 3-keto-desogestrel, also known as etonogestrel, which is the active drug substance (Ref. II). Therefore, all environmental data are based on the active drug substance, etonogestrel.

Ecotoxicological studies

Crustacean, water flea *(Daphnia magna)* (FDA TAD 4.08) (Ref. III):
Acute toxicity
EC50 48h (mortality) = 3900 µg/L

Fish, rainbow trout *(Oncorhynchus mykiss)* (FDA TAD 4.11) (Ref. IV)*:*
Acute toxicity
LC50 96h (mortality) = 4000 µg/L

Fish, bluegill sunfish *(Lepomis macrochirus)* (OECD 203) (Ref. V)*:*
Acute toxicity
LC50 96h (mortality) > 1300 µg/L

Green Algae *(Selenastrum capricornutum)* (FDA TAD 4.01) (Ref. VI)*:*
EC50 8d (yield & growth rate) > 5400 µg/L
NOEC 8d (yield & growth rate) = 5400 µg/L

Green Algae *(Selenastrum capricornutum)* (FDA TAD 4.01) (Ref. VI)*:*
EC50 8d (yield & growth rate) > 4500 µg/L
NOEC 8d (yield & growth rate) = 4500 µg/L

Crustacean, water flea *(Daphnia magna)* (FDA TAD 4.09) (Ref. VII):
Chronic toxicity
NOEC 21d (immobilization and growth) = 1200 µg/L
LOEC 21d (immobilization and growth) = 2400 µg/L

Fish, fathead minnow *(Pimephales promelas)* (OECD 210) (Ref. VIII):
Chronic toxicity
NOEC 32d (total length and dry weight) = 59 µg/L
LOEC 32d (total length and dry weight) = 120 µg/L

Fish, Japanese medaka *(Oryzias latipes)* (OECD 229 & Draft Fish Two-generation Test Guideline) (Ref. IX):
Chronic toxicity
NOEC 183d (genetic sex ratio of XX males to the total number of male fish) = 2.7 ng/L
LOEC 183d (genetic sex ratio of XX males to the total number of male fish) = 6.2 ng/L

PNEC = 0.00027 ug/L (2.7 ng/L / 10 based on the most sensitive chronic NOEC for the fish and an assessment factor (AF) of 10)

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.0005/0.00027 = 2, i.e. 1 < PEC/PNEC < 10 which justifies the phrase for the prodrug (desogestrel) of "Use of desogestrel has been considered to result in moderate environmental risk."

Biotic degradation

Biodegradation Simulation Screening (US FDA 3.11) (Ref. X):
Test results 3.6% degradation in 37 days in water, with a calculated half-life of 457 days

Biodegradation Simulation Screening (US FDA 3.12) (Ref. XI):
Half-life in sediment = 83 – 219 days. Degradation in sludge = 96% in 13 days

Biodegradation Simulation Screening (FDA TAD 3.12) (Ref. XII):
Half-life = 19 - 106 days in soil

Sediment Transformation (OECD 308) (Ref. XIII):
DT_{50} (total system) = 9.2 to 50 days

At each sampling interval, duplicate incubation vessels per sediment/water system were removed from incubation chamber and water layers were separated from sediment layers. The two layers were analyzed separately for [^{14}C]etonogestrel and degradates. The sediment was extracted once with acetonitrile (80:20:0.1, v:v:v) for a total of three extractions. The water and sediment extracts were radioassayed by liquid scintillation counting (LSC) and then analyzed by high performance liquid chromatography with radiochemical detection (HPLC/RAM) to quantify [14C]etonogestrel and degradation products in the fractions. Radioactivity in the post-extracted solids (sediment-non-extractable residues (NER)) was quantified by combustion analysis and the liquid volatile organic traps were radioassayed by LSC.

Average material balance ranged from 94.9 to 107.0% AR over the course of the 99 day study.
Evidence of primary biodegradation was observed for [^{14}C] etonogestrel in the aerobic water/sediment test samples. Two major peaks (≥ 10% AR) were observed in some of the chromatograms for the Taunton River and Weweantic River samples at retention times of 20.9 (Met-1) and 23.1 minutes (Met-2). Several minor peaks were observed in some of the chromatograms for the Taunton River and Weweantic River test samples. In all cases, these minor peaks represented less than 10% AR in the water and sediment extracts and were not considered further.
Ultimate biodegradation of [^{14}C] etonogestrel was observed in the aerobic samples with evolution of $^{14}CO_2$ reaching an average maximum of 1.2 and 5.3% AR for the Taunton River and Weweantic River aerobic test samples, respectively, at Day 99. Radioactivity was not detected in the volatile organic compound traps for the aerobic test systems accumulatively at Day 99.

Abiotic degradation

Photolysis (US FDA 3.10) (Ref. XIV):
Half-life = 61.7 hours

Hydrolysis (US FDA 3.09) (Ref. XV):
Hydrolytically stable, <10% degradation at pH 5, 7, 9

Justification of chosen degradation phrase:
Etonogestrel has a DT_{50} for the total system of ≤120 days. Thus, the phrase chosen for the prodrug (desogestrel) is “Desogestrel is slowly degraded in the environment.”

Bioaccumulation

Partitioning coefficient (FDA TAD 3.02) (Ref. VXI):
Log Kow = 3.5

Bioaccumulation (OECD 305) (Ref. VXII):
Flow through study with Bluegill sunfish (*Lepomis macrochirus*)
Lipid normalized kinetic BCF = 128

Justification of chosen bioaccumulation phrase:
Since log Kow < 4 and BCF < 500, the substance has low potential for bioaccumulation

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