FASS

ZYTIGA

MRx EF

Janssen

Filmdragerad tablett 500 mg

(Violetta, ovala, filmdragerade tabletter (20 mm långa och 10 mm breda), präglade med ”AA” på ena sidan och ”500” på andra sidan)

Endokrin terapi, övriga antihormoner och relaterade medel

Aktiv substans:

Abirateronacetat

ATC-kod:

L02BX03

Läkemedel från Janssen omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Abirateron

Miljörisk: Användning av abirateron har bedömts medföra hög risk för miljöpåverkan.
Nedbrytning: Abirateron bryts ned i miljön.
Bioackumulering: Abirateron har hög potential att bioackumuleras.

Detaljerad miljöinformation

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

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

PEC = 0.05211206 µg/L

Where:

A	=	total actual API sales in Sweden for the most recent year 380.3800 (total sold amount API in the most recent sales data for Sweden (2020) was distributed by IQVIA in 2021)
R	=	0
P	=	number of inhabitants in Sweden = $10 * 10^6$
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 (Pseudokirchneriella subcapitata) (guideline eg OECD 201) [Reference II]

$E\gamma C_{50}$ 72 h (yield inhibition) > 1.0 mg/L
NOECγ (yield inhibition) = 1.0 mg/L
E_rC_{50} 72 h (growth rate) > 1.0 mg/L
$NOEC_r$ (growth rate) = 1.0 mg/L

Crustacean (Daphnia magna) (water-flea):

Acute toxicity
LC_{50} 96 h = 0.25 mg/L (guideline eg OECD 202) (Reference III)
NOEC = < 0.048 mg/L

Chronic toxicity
NOEC 21 days (Reproduction and Growth) = 0.47 µg/L (guideline eg OECD 211) (Reference IV)

Fish:
Acute toxicity

Oncorhynchuss mykiss (rainbow trout)

LC_{50} 96 h = 0.13 mg/L (guideline eg OECD 203) (Reference V)
NOEC = 0.065 mg/L

Chronic toxicity

Pimephales promelas (fathead minnow)

Fish early life stage test
NOEC 35 days (Total body length) = 1.1 µg/L (guideline eg OECD 210) (Reference VI)

Fish partial life cycle study
NOEC 119 days (Number of spawns per female) = 13 ηg/L (guideline eg OECD 229) (Reference VII)

Other ecotoxicity data:

Activated sludge respiration inhibition test according to guideline eg OECD 209 (Reference VIII)
EC_{50} 3h > 1000 mg/L
NOEC 3h ≥ 1000 mg/L

PNEC (µg/l) = lowest NOEC/10, where 10 is the assessment factor used. NOEC for fathead minnow *Pimephales promelas* of 13 ηg/L has been used for this calculation since it is the most sensitive of the three tested species.

PNEC = 13 ηg/L/10 = 1.3 ηg/L = 0.0013 µg/L

Environmental risk classification (PEC/PNEC ratio)
PEC/PNEC = 0.05211206 µg/L /0.0013 µg/L = 40.0862

i.e. PEC/PNEC > 10 which justifies the phrase 'Use of Abiraterone acetate has been considered to result in high environmental risk.

Degradation
Biotic degradation

Ready degradability:

According to guideline eg OECD 301B (Reference IX):
Abiraterone acetate was investigated for its ready biodegradation in a 28-day CO_2-evolution test.
Result: Not readily biodegradable.

Inherent degradability: -

Simulation studies:

Aerobic degradation in aquatic sediment systems according to guideline eg OECD 308 (Reference X):

Abiraterone acetate was investigated for its aerobic degradation in a 101-day aquatic sediment test.

For analysis the sediment was extracted once with acetonitrile, once with acetonitrile:trifluoroacetic acid 100:0.5 (v:v) and once (twice
on Day 101) with acetonitrile:water:trifluoroacetic acid 80:20:0.5, (v:v:v) for a maximum of four extractions.
The water and sediment extracts were radioassayed by LSC and then analyzed by HPLC/RAM to quantify [^{14}C]abiraterone

acetate and degradation products in the fractions. The radioactivity in the post extracted solids (sediment bound) were quantified by combustion analysis. The volatile organic traps were radioassayed by LSC.

The rates of dissipation (DT_{50} and DT_{90}) of Abiraterone acetate from the water phase and the entire system were calculated using first order kinetics:

System	Water		Total system	
	DT_{50} (Days)	DT_{90} (Days)	DT_{50} (Days)	DT_{90} (Days)
Taunton River Aerobic	2.3	7.7	4.9	16
Weweantic River Aerobic	2.3	7.6	3.3	11

In aerobic aquatic sediment systems, Abiraterone acetate rapidly dissipated from the water phase by adsorption to the sediment.

Abiraterone acetate is degraded in the environment.

Abiotic degradation

Hydrolysis: -
Photolysis: -

Bioaccumulation

Partition coefficient octanol/water:

The partition coefficient octanol/water was determined according to guideline eg OECD 117 [Reference XI]:

Log D_{ow} >6.20 (pH = 6.10)

Bioconcentration factor (BCF):

The bioconcentration and depuration characteristics of Abiraterone acetate in the rainbow trout in a flow through system were examined according to EMA's assessment report [Reference XII].

BCF_{low} dose = 903
BCF_{high} dose = 931

The BCF value of the low and high dose indicates that Abiraterone acetate has high potential to bioconcentrate in the rainbow trout.

Since BCF > 500, Abiraterone acetate has high potential for bioaccumulation.

Excretion (metabolism)

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PBT/vPvB assessment

	PBT-criteria	Results for Abiraterone acetate
Persistence	Half-life in freshwater: DT_{50} > 40 days Half-life in sediment: DT_{50} > 120 days	$DT_{50,river}$ = 2.3 days $DT_{50,system}$ = 4.9 days
Bioaccumulation	BCF > 2000	BCF = 903 (low dose) and 931 (high dose)
Toxicity	Chronic NOEC < 10 µg/L	$NOEC_{algae}$ = 1.0 mg/L $NOEC_{daphnia}$ = 0.47 µg/L $NOEC_{fish}$ = 13 ηg/L

According to the established EU-criteria Abiraterone acetate should not be regarded as a PBT substance.

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