FASS

Kaletra

AbbVie

Oral lösning (80 mg + 20 mg) /ml
(ljusgul till guldfärgad)

Virushämmande medel för systemiskt bruk

Aktiva substanser (i bokstavsordning):
Lopinavir
Ritonavir

ATC-kod:
J05AR10

Läkemedel från AbbVie omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Lopinavir

Miljörisk: Användning av lopinavir har bedömts medföra försumbar risk för miljöpåverkan.
Nedbrytning: Det kan inte uteslutas att lopinavir är persistent, då data saknas.
Bioackumulering: Lopinavir har hög potential att bioackumuleras.

Detaljerad miljöinformation

Environmental Risk Classification

Predicted Environmental Concentration (PEC) (Ref. 1)
PEC is calculated according to the following formula:
PEC (µg/L) = $(A*10^9*(100-R))/(365*P*V*D*100)$
Where:

A (kg/yr)	7.75	Total sold amount API in Sweden year 2022, data from IQVIA (Ref. 2)
R (%)	0	

		Removal rate (due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation); use 0 if no data is available (Ref. 1)
P	$10*10^6$	Number of inhabitants in Sweden
V (L/day)	200	Volume of wastewater per capita and day (default value) (Ref. 1,3)
D	10	Factor for dilution of wastewater by surface water flow (default value) (Ref. 1, 3)

(Note: the factor 10^9 converts the quantity (A) from kg to µg).

PEC (µg/L) = $(7.75*10^9*(100-0))/(365*10*10^6*200*10*100)$
PEC = 0.00106 µg/L

Predicted No Effect Concentration (PNEC)

PNEC: Not determined; no ecotoxicology data is available.

Ecotoxicological Studies with Lopinavir

Short-term ecotoxicology studies were not available for lopinavir, but physico-chemical, environmental fate and ecotoxicology data were modelled based on measured data for ritonavir, a compound with a similar structural core. The relevance of the modelled data presented below is considered questionable due to the outdated version of software used to generate the data (ECOSAR V 0.99e) and the actual structural similarity of lopinavir and ritonavir. Generation of updated ecotoxicology data for lopinavir are being pursued. No observable effect concentrations (NOEC) were generated since the ritonavir studies from which the modelling was based resulted in NOECs at the maximum concentration evaluated. Due to the uncertainty regarding the validity of the modelled data, a conservative risk summary phrase was chosen.
Algae (Green Algae): Acute toxicity
EC_{50} 96 h (growth) = 1.914 mg/L (1914 µg/L) (Ref. 4)
Crustacean (*Daphnia magna*): Acute toxicity
LC_{50} 48 h (immobilization) = 2.652 mg/L (2652 µg/L) (Ref. 4)
Fish (*Lepomis macrochirus*): Acute toxicity
LC_{50} 96 h (lethality) = 2.082 mg/L (2082 µg/L) (Ref. 4)

Environmental Risk Classification (PEC/PNEC ratio)

According to the European Medicines Agency guideline on environmental risk assessment of medicinal products (EMA/CHMP/SWP/4447/00), use of lopinavir is unlikely to represent a risk for the environment, because the predicted environmental concentration (PEC) is below the action limit 0.01 µg/L.

Degradation

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

Justification of chosen biodegradation phrase:

No degradation data could be found. Therefore, the potential for persistence of lopinavir cannot be excluded due to lack of data.

Bioaccumulation

Lopinavir has high potential for bioaccumulation.

Log D_{ow} (Octanol Water Coefficient) = 4.7 (pH 7.4) (25°C) (Refs. 4 and 5)

The method used to derive the Log D_{ow} is unknown.

Justification of chosen bioaccumulation phrase:

Log D_{ow} = 4.7. As the log D_{ow} is ≥ 4.0, lopinavir has high potential for bioaccumulation.

Excretion and Pharmacological Activity

Lopinavir is excreted up to 22.0% as parent and up to 78% as metabolites. The parent compound and metabolite composition in excreta (urine and feces) was as follows: lopinavir, M-1, M-3/4, M-6 to M-8, M-9/10, M-l 1 to M-15, with the remaining radioactivity present as several unknown metabolites. (Ref. 6)

The *in vitro* antiviral activity for all metabolites is unknown except for two metabolites which have potency comparable to that of the parent drug. (Refs.7).

References

1. FASS.se. Environmental classification of pharmaceuticals at www.fass.se. Guidance for pharmaceutical companies. 2012 V 2.0. 2021.
2. IQVIA. 2022. IQVIA / LIF - kg consumption/2022.
3. European Chemicals Agency (ECHA). Guidance on Information Requirements and Chemical Safety Assessment Chapter R.16: Environmental exposure assessment. Version 3.0. 2016.
4. Huntingdon Life Sciences. Environmental Risk Assessment of Lopinavir. November 2005.
5. Abbott. Abbott-157378 and Abbott-84538 (Ritonavir) Product Development Report. Preliminary Physical and Chemical Characterization of Abbott-157378 and Comparison with Abbott-84538 (Ritonavir). R&D/95/972. December 1995.
6. Abbott. Abbott-157378 Drug Metabolism Report No. 44 Metabolism and Disposition of [^{14}C]ABT-378 Given in Combination with Ritonavir in Healthy Male Subjects Following a Single Oral Administration Protocol M97-723. R&D/99/031. January 1999.
7. Abbott. Abbott-157378 Drug Metabolism Report No. 57 Overview of Absorption, Distribution, Metabolism and Excretion of ABT-378 (Abbott-157378) in Animals. R&D/99/652. December 1999.