FASS

Kyprolis

MRx EF

Amgen

Pulver till infusionsvätska, lösning 10 mg
(Vitt till benvitt frystorkat pulver)

Antineoplastiska medel

Aktiv substans:
Karfilzomib

ATC-kod:
L01XX45

Läkemedel från Amgen omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Karfilzomib

Miljörisk: Risk för miljöpåverkan av karfilzomib kan inte uteslutas då ekotoxikologiska data saknas.
Nedbrytning: Det kan inte uteslutas att karfilzomib är persistent, då data saknas.
Bioackumulering: Karfilzomib har hög potential att bioackumuleras.

Detaljerad miljöinformation

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula (FASS, 2012, p. 11): PEC (µg/L) = (A x 10^9 x (100-R))/(365 x P x V x D x 100) = 1.5x10^{-6} x A x (100-R) where:

A = 0.4 kg x 0.5% = 2 x 10^{-3} Kg =total sold amount API in Sweden year 2017, data from IQVIA 2018 adjusted, based on metabolism data (<0.5% Carfilzomib detected in excreta of patients).

R = 0 % removal rate (due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation), = 0, if no data is available.

P = number of inhabitants in Sweden = 9 x10^6

V (L/day) = volume of wastewater per capita and day = 200 (ECHA default) (ECHA, 2008)

D = factor for dilution of waste water by surface water flow = 10 (ECHA default) (ECHA, 2008)

PEC (µg/L) = 1.5 x 10^{-6} x 2 x10^{-3}x (100)

PEC = 3x10^{-7}µg/L

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

No ecotoxicity data are available.

Environmental risk classification (PEC/PNEC ratio)

As there are no data to calculate the PEC/PNEC ratio the phrase: "Risk of environmental impact of carfilzomib cannot be excluded, since no ecotoxicity data are available." is used. However, use of carfilzomib is unlikely to represent a risk for the environment, because the predicted environmental concentration (PEC) is more than 10,000 times below the European Medicines Agency’s action

limit 0.01 µg/L stated in its guideline on environmental risk assessment (EMEA, 2006).

Degradation

No degradation data are currently available. However, the applicant is currently conducting a laboratory study of the transformation of carfilzomib in aquatic sediments (OECD 308). As no degradation data are currently available the phrase:
"The potential for persistence of carfilzomib cannot be excluded due to lack of data" is used.

Abiotic degradation

No abiotic degradation data are available.

Bioaccumulation

Partitioning coefficient:
Data from OECD 107 Study: Octanol/Water Partition Coefficient of carfilzomib*

Buffer Solution	P_{ow} ¶	$\log_{10} P_{ow}$ ¶
pH 4	3580	3.6
pH 7	40100	4.6
pH 9	29000	4.5

*(ENVIGO, 2015)

As log Dow > 4 at pH 7 the phrase:
"Carfilzomib has high potential for bioaccumulation." is used.

Excretion (metabolism)

The reduction of 1 kg (total sold amount API in Sweden year 2020, data from Amgen (projected sales)) by a factor of 200 (i.e., 1/0.5%) in the PEC calculation based on metabolism is justified as follows. Carfilzomib was rapidly and extensively metabolized. The predominant metabolites measured in human plasma and urine, and generated *in vitro* by human hepatocytes, were peptide fragments and the diol of carfilzomib, suggesting that peptidase cleavage and epoxide hydrolysis were the principal pathways of metabolism. Cytochrome P450-mediated mechanisms played a minor role in overall carfilzomib metabolism. Carfilzomib is excreted to 0.5% as parent compound and up to 35% as quantifiable metabolites in urine. The metabolites have no known pharmacological activity (Wang et al., 2013).

PBT/vPvB assessment

Carfilzomib does not fulfil the criteria for PBT and/or vBvP classification as no data is available.

References

ECHA. (2008). Guidance on Information Requirements and Chemical Safety Assessment. Helsinki, Finland: European Chemicals Agency.

EMEA. (2006). Guideline on the Environmental Risk Assessment of Medicinal Products for Human Use (EMEA CHMP/SWP/4447/00 corr 2). London, UK: European Medicines Evaluation Agency, Committee for Medicinal Products for Human Use (CHMP). ENVIGO. (2015). Carfilzomib Partition Coefficient (Envigo Study Number: DZL0024). Suffolk, UK: Envigo CRS Limited.

FASS, (2012). Environmental classification of pharmaceuticals in www.fass.se – guidance for pharmaceutical companies.

Wang, Z., Yang, J., Kirk, C., Fang, Y., Alsina, M., Badros, A., Papadopoulos, K., Wong, A., Woo, T., Bomba, D., Li, J., & Infante, J. R. (2013). Clinical pharmacokinetics, metabolism, and drug-drug interaction of carfilzomib. Drug Metab Dispos, 41(1), 230-237.