FASS

Avamys

GlaxoSmithKline

Nässpray, suspension 27,5 mikrogram/spraydos
(Vit)

Nasala preparat, kortikosteroider.

Aktiv substans:
Flutikasonfuroat

ATC-kod:
R01AD12

Läkemedel från GlaxoSmithKline omfattas av Läkemedelsförsäkringen.
Läkemedlet distribueras också av företag som inte omfattas av Läkemedelsförsäkringen, se Förpackningar.

Miljöpåverkan

fluticasone furoate

Miljörisk: Användning av fluticasone furoate har bedömts medföra försumbar risk för miljöpåverkan.
Nedbrytning: fluticasone furoate är potentiellt persistent.
Bioackumulering: fluticasone furoate 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) = $(A*10^{9}*(100-R))/(365*P*V*D*100) = 1.37*10^{-6}$ *A(100-R)
PEC = 9.98 $x10^{-5}$ µg/L

Where:
A = 0.7280 kg (total sold amount API in Sweden year 2021, data from IQVIA Health).
R = 0% removal rate (conservatively, it has been assumed there is no loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation).
P = number of inhabitants in Sweden = $10*10^{6}$
V (L/day) = volume of wastewater per capita and day = 200 (ECHA default) (Reference 1)
D = factor for dilution of waste water by surface water flow = 10 (ECHA default) (Reference 1)

Predicted No Effect Concentration (PNEC)

Ecotoxicological studies

Algae:

No data

Water flea (Daphnia magna):
Acute toxicity
EC50 48 h (immobility) > 12 µg/L (OECD 202) (Reference 4)
NOEC = 12 µg/L
Chronic toxicity
No data

Fish (Pimephales promelas):
Acute toxicity
No data
Chronic toxicity
LOEC 116 days > 0.58 µg/L (OECD 210/234) (Reference 8)
NOEC = 0.58 µg/L

Other ecotoxicity data:

Microorganisms in activated sludge:
EC50 3 h (inhibition) > 1,000,000 µg/L @ 3 hrs (OECD 209) (Reference 4)

Earthworm (*Eisenia foetida*):
LC50 14 days (lethality) > 1,000,000 µg/kg (OECD 207) (Reference 5)
NOEC = 1,000,000 µg/Kg
PNEC = 0.58/10 = 0.058 µg/L

PNEC (µg/L) = lowest NOEC/10, where 10 is the assessment factor applied for one long-term NOECs but where there is a high degree of confidence that the dataset includes the most sensitive species

(fish) and addresses the specific mode of action (endocrine disruption). On this basis the NOEC for fish has been used in the calculation.

PNEC Justification

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

However, fluticasone furoate is a glucocorticoid and, as such, is considered as a potential endocrine active substance and therefore the potential endocrine activity of this compound was investigated in an appropriate chronic vertebrate test system with relevant end points. Accordingly, GSK has conducted a fish early life-stage test, as per OECD 210, as a range-finder to set concentrations for an extended early life-stage test, exposing newly fertilised embryos until they reached sexual maturity (OECD 234). This study concluded that no statistically significant effects were observed between the controls and any of the test concentrations in terms of hatching success, post-hatch survival, growth, spawning ability or secondary sexual characteristics. Due to the mode of action of fluticasone furoate and its potential to act as an endocrine active substance there is a high degree of confidence that fish is the most sensitive species and on that basis there is a strong justification for applying an AF of 10 (Reference 1).

Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 9.98 $x10^{-5}$ /0.058 = 1.72 $x10^{-3}$, i.e. PEC/PNEC ≤ 0.1 which justifies the phrase “Use of fluticasone furoate has been considered to result in insignificant environmental risk.”

Degradation

Biotic degradation

Ready degradability:

No Data

Inherent degradability:

0% degradation in 28 days (OECD 302C) (Reference 7)

Soil Metabolism:

3% degradation in 64 days (OECD 304) (Reference 6)

Abiotic degradation

Hydrolysis:

No data

Photolysis:

No data

Justification of chosen degradation phrase:

Fluticasone furoate is not readily degradable or inherently degradable but it is slowly degraded in soil. The phrase “fluticasone furoate is potentially persistent” is thus chosen.

Bioaccumulation

Partitioning coefficient:

Log Kow = 2.61 at pH 7 (OECD 117) (Reference 5)

Justification of chosen bioaccumulation phrase:

Since log Kow < 4 at pH 7, the substance has a low potential for bioaccumulation.

Excretion (metabolism)

Fluticasone furoate is rapidly cleared (total plasma clearance of 58.7 l/h) from systemic circulation principally by hepatic metabolism to an inactive 17β-carboxylic metabolite (GW694301X), by the cytochrome P450 enzyme CYP3A4. The principal route of metabolism was hydrolysis of the S-fluoromethyl carbothioate function to form the 17β-carboxylic acid metabolite. In vivo studies have revealed no evidence of cleavage of the furoate moiety to form fluticasone.

Elimination was primarily via the faecal route following oral and intravenous administration indicative of excretion of fluticasone furoate and its metabolites via the bile. Following intravenous administration, the elimination phase half-life averaged 15.1 hours. Urinary excretion accounted for approximately 1 % and 2 % of the orally and intravenously administered dose, respectively. (Reference 2).

PBT/vPvB assessment

Fluticasone furoate does not fulfil the criteria for PBT and/or vPvB All three properties, i.e. ‘P’, ‘B’ and ‘T’ are required in order to classify a compound as PBT (Reference 1). Fluticasone furoate does not fulfil the criteria for PBT and/or vBvP based on log Pow < 4.

Please, also see Safety data sheets on http://www.msds-gsk.com/ExtMSDSlist.asp.

References:

1. ECHA, European Chemicals Agency. 2008 Guidance on information requirements and chemical safety assessment.
2. Pharmacokinetic properties: Meatbolism and Elimination. Summary of Product Characteristics Avamys (fluticasone furoate). GlaxoSmithKline, January 2016.
3. Burwood CE. GW685698X: Determination of Inhibition of Respiration of Activated Sludge. Report No. 1990/363. GlaxoSmithKline, June 2004.
4. Manson P. GW685698X: Acute toxicity to *Daphnia magna*. Report No. 1990/369. GlaxoSmithKline, November 2004.
5. Swales S. Acute toxicity of GW685698X to the earthworm *Eisenia fetida*. Report No. 1990/383. GlaxoSmithKline, April 2004.
6. Krajewski M. (14C)-GW685698X: Inherent Biodegradability in Soil Report No. 1990/384. GlaxoSmithKline, June 2004.
7. Mead C and McKenzie J. GW685698X: Assessment of Inherent Biodegradability; Modified MITI (II) Test. Report No. 813/735 GlaxoSmithKline, October 2004
8. Goodband T. Extended Fish Early Life Stage Test (*Pimephales promelas*). Report No. 3200560. GlaxoSmithKline, March 2016.