

Bofunir

M

Sandoz AS

Inhalationspulver, avdelad dos 320 mikrogram/9 mikrogram/inhalation

Avregistreringsdatum: 2023-06-15 (Tillhandahålls ej)

Aktiva substanser (i bokstavsordning):

Budesonid

Formoterol

ATC-kod:

R03AK07

För information om det avregistrerade läkemedlet omfattas av Läkemedelsförsäkringen, kontakta Läkemedelsförsäkringen.

Läs mer om avregistrerade läkemedel

Miljöpåverkan

Miljöinformationen för formoterol är framtagen av företaget AstraZeneca för Bevespi Aerosphere, Budfor, Edoflo, Eltren, Eltren forte, Eltren mite, Gardette, Gardette forte, Gardette mite, Oxis® Turbuhaler®, Riltrava Aerosphere, Symbicort, Symbicort® Turbuhaler®, Symbicort® forte Turbuhaler®, Symbicort® mite Turbuhaler®, Trixeo Aerosphere

Miljörisk: Användning av formoterol har bedömts medföra försumbar risk för miljöpåverkan.

Nedbrytning: Formoterol är potentiellt persistent.

Bioackumulering: Formoterol har låg potential att bioackumuleras.

Detaljerad miljöinformation

$$PEC/PNEC = 0.000050 \mu\text{g/L} / 94 \mu\text{g/L} = 0.5 \cdot 10^{-7}$$

$$PEC/PNEC \leq 0.1$$

Environmental Risk Classification

Predicted Environmental Concentration (PEC)

The PEC is based on the following calculation:

$$\text{PEC } (\mu\text{g/L}) = (A \cdot 10^9 \cdot (100 - R)) / (365 \cdot P \cdot V \cdot D \cdot 100)$$

$$\text{PEC } (\mu\text{g/L}) = 1.37 \cdot 10^{-6} \cdot A \cdot (100 - R)$$

$$\text{PEC} = 1.37 \cdot 10^{-6} \cdot 0.34 \cdot (100 - 0)$$

$$= \underline{0.000050 \mu\text{g/L}}$$

Where;

A (kg/year) = total sold amount API in Sweden year 2020, data from IQVIA

= 0.34 kg

R (%) = removal rate (due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation)

= 0%

P = number of inhabitants in Sweden

= $10 \cdot 10^6$

V (L/day) = volume of wastewater per capita and day

= 200 L/day (Ref 1)

D = factor for dilution of waste water by surface water flow

= 10 (Ref 1)

Note: The factor 10^9 converts the quantity used from kg to μg .

Metabolism and excretion

The major part of the dose of formoterol fumarate dihydrate is eliminated via metabolism. After inhalation, 8-13% of the delivered dose is excreted unmetabolised in the urine. (Ref 2).

Ecotoxicity Data

Study Type	Method	Result	Reference
Toxicity to green algae, <i>Scenedesmus capricornutum</i> , growth inhibition test	OECD201	72 hour NOEC _{growth rate} = 30 mg/L 72 hour LOEC _{growth rate} = 60 mg/L 72 hour EC50 _{growth rate} = 94 mg/L 72 hour NOEC _{biomass} = 15 mg/L 72 hour LOEC _{biomass} = 30 mg/L 72 hour EC50 _{biomass} = 46 mg/L	3
Acute toxicity to <i>Daphnia magna</i>	OECD202	48 hour NOEC = 55 mg/L 48 Hour EC50 = 144 mg/L	4
Acute toxicity to rainbow trout, <i>Oncorhynchus mykiss</i>	OECD203	96 hour NOEC = 120 mg/L 96 hour EC50 > 120 mg/L	5

Predicted No Effect Concentration (PNEC)

Short-term tests have been undertaken for species from three trophic levels, based on internationally accepted guidelines. The most sensitive species of these is the green alga, *Pseudokirchneriella subcapitata* (formerly known as *Selenastrum capricornutum*), and the growth rate end point has been applied. Therefore, the PNEC is based on the growth rate results (EC50) from the toxicity to *P subcapitata* study, and an assessment factor of 1000 is applied in accordance with ECHA guidance (Ref 6).

$$\text{PNEC} = 94\,000/1000 = 94 \mu\text{g/L}$$

Environmental risk classification (PEC/PNEC ratio)

$$\text{PEC/PNEC} = 0.000050 \mu\text{g/L} / 94 \mu\text{g/L} = 0.5 \cdot 10^{-7}$$

$$\text{PEC/PNEC} \leq 0.1$$

The PEC/PNEC ratio decides the wording of the aquatic environmental risk phrase, and the risk phrase for $\text{PEC/PNEC} \leq 0.1$ reads as follows: "Use of formoterol fumarate dihydrate has been considered to result in insignificant environmental risk".

In Swedish: "Användning av formoterol fumarat dihydrat har bedömts medföra försumbar risk för miljöpåverkan" under the heading "Miljörisk".

Environmental Fate Data

Study Type	Method	Result	Reference
Aerobic biodegradation	ISO 8727-1984E	20.5% biodegradation after 28 days. Not readily biodegradable	6

Physical Chemistry Data

Study Type	Method	Result	Reference
Octanol-water distribution coefficient	Shake flask	pH 5 $\log D_{OW} = 0.146$ pH 7 $\log D_{OW} = 1.18$ pH 9 $\log D_{OW} = 7.85$	7
Dissociation Constant	Potentiometric titration	pKa = 7.9 (Phenol) pKa = 9.2 (Amine)	8

Biodegradation

Based on the data above and lack of further studies, the phrase "Formoterol fumarate dihydrate is potentially persistent" is chosen.

In Swedish: "Formoterol fumarat dihydrat är potentiellt persistent" under the heading "Nedbrytning".

Bioaccumulation

Partition coefficient Octanol/Water

Log D = 1.18 at pH 7

Since Log D < 4 the phrase 'Formoterol fumarate dihydrate has low potential for bioaccumulation' is assigned.

In Swedish: "Formoterol fumarat dihydrat har låg potential att bioackumuleras" under the heading "Bioackumulering".

References

1. [ECHA] European Chemicals Agency. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.16: Environmental exposure assessment (version 3.0). February 2016.
2. Determination of absolute pulmonary bioavailability of formoterol when given via Turbuhaler® to healthy volunteers. Report No. 37-CR-3004. January 1995.
3. Formoterol Fumarate Dihydrate: Toxicity to the green alga *Selenastrum capricornutum*. Brixham Environmental Laboratory, AstraZeneca, UK. Report BL8081 (2005).
4. Formoterol Fumarate Dihydrate: Acute toxicity to *Daphnia magna*. Brixham Environmental Laboratory, AstraZeneca, UK Report BL8082 (2005).
5. Formoterol Fumarate Dihydrate: Acute toxicity to Rainbow Trout (*Oncorhynchus mykiss*). Brixham Environmental Laboratory, AstraZeneca, UK. Report BL8083 (2005).
6. A026: Biodegradability. Report no: 59/93, Toxicon, Landskrona, Sweden. 10 January 1994
7. Determination of the n-octanol/Water Partition Coefficient of Formoterol Fumarate by the Shake Flask Method, 123K-104, EAG, Inc., Easton, Maryland 2017
8. Marketing, S1-03 general Properties, Formoterol Fumarate Dihydrate. AstraZeneca report BD4179 (2009).