FASS

Daktacort®

M (℞) Ff

McNeil

Kräm 20 mg/g + 10 mg/g
(vit, luktfri kräm)

Utvärtes medel vid hudmykoser, kombinationer

Aktiva substanser:
Hydrokortison
Mikonazol

ATC-kod:
D01AC20

Läkemedel från McNeil omfattas av Läkemedelsförsäkringen.

Miljöpåverkan

Hydrokortison

Miljörisk: Risk för miljöpåverkan av hydrokortison kan inte uteslutas då ekotoxikologiska data saknas.
Nedbrytning: Det kan inte uteslutas att hydrokortison är persistent, då data saknas.
Bioackumulering: Det kan inte uteslutas att hydrokortison kan bioackumuleras, då data saknas.

Mikonazol

Miljörisk: Användning av mikonazol har bedömts medföra låg risk för miljöpåverkan.
Nedbrytning: Mikonazol är potentiellt persistent.
Bioackumulering: Mikonazol har hög potential att bioackumuleras.

Detaljerad miljöinformation

1. PREDICTED ENVIRONMENTAL CONCENTRATION (PEC):
The Predicted Environmental Concentration is calculated using the following formula:

PEC (µg/L) = A x 10^9 x (100 – R) / 365 x P x V x D x 100
Where:

A (kg/year)	=	total actual API sales (API) in Sweden for the most recent year (obtained from LIF 454.1803 kg (total sold amount API in Sweden in 2015, data from IMS Health) {10}
R (%)	=	removal rate (due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation)
	=	0% (worst-case scenario: no removal)
P	=	number of inhabitants in Sweden (9 x 10^6)
V (L/day)	=	volume of waste water per capita and day
	=	200 (ECHA default) {11}
D	=	factor for dilution of waste water by surface water flow
	=	10 (ECHA default) {11}
PEC (µg/L)	=	0.0691 µg/L

2. PREDICTED NO EFFECT CONCENTRATION (PNEC):

2.1. Ecotoxicological studies

Algae (*Selenastrum capricornutum*) (OECD No. 201) {1}:
E_rC_{50} 72 h = 30 µg/L
$NOEC_r$ 72 h = 10 µg/L

Crustacean (*Daphnia magna*) (OECD No. 202) {2}:
Acute toxicity / EC_{50} 48 h = 119 µg/L

Fish (*Brachydanio rerio*) (OECD No. 203) {3}:
Acute toxicity / LC_{50} 96 h = 144 µg/L

Fish (*Brachydanio rerio*) (OECD No. 204) {4}:
Chronic toxicity / NOEC (21 days) = 12 µg/L

Fish (*Oncorhynchus mykiss*) (OECD No. 215) {5}:
Chronic toxicity / NOEC (28 days) = 20 µg/L

Other ecotoxicity data: Activated sludge respiration inhibition test (OECD No. 209) {6}:
EC_{50} 3 h > 1000 mg/L

NOEC 3 h ≥ 1000 mg/L

2.2. Calculation of Predicted No Effect Concentration (PNEC)

PNEC (µg/l) = lowest NOEC/50, where 50 is the assessment factor used. The $NOEC_r$ for the green algae *Selenastrum capricornutum* 10 µg/L has been used for this calculation since it is the most sensitive of the three tested species.

PNEC = 10 µg/L/50 = 0.2 µg/L

2.3. Environmental risk classification (PEC/PNEC ratio)

PEC/PNEC = 0.0691 µg/L / 0.2 µg/L = 0.3455, i.e. 0.1 < PEC/PNEC ≤ 1
Use of miconazole nitrate has been considered to result in low environmental risk.

3. DEGRADATION

3.1. Biotic degradation

Ready biodegradation (OECD No. 301F) {7}:
The ready biodegradability test indicated that miconazole nitrate is not readily biodegradable.

3.2. Abiotic degradation

Photodegradation (OECD draft) {8}:
The rate of photo-chemical degradation of ^{14}C-miconazole nitrate was investigated in natural marine water and in sterile purified water. A pre-test showed that the parent compound was rapidly degraded after 5 days in both systems. Consequently, a main test was performed for a longer period of 15 days, corresponding to at least 30 days of natural sunlight.

In the main test, miconazole nitrate rapidly photo-degraded from an initial amount of 100% to 4.8% in marine water and to 43.9% in purified water after 5 days of continuous irradiation. At the end of irradiation (15 days), miconazole nitrate was no longer detected in marine water and represented only 2.8% of the applied radioactivity in purified water.

Besides the parent compound, up to 21 photo-degradates were detected in the main test of which two were characterized by co-chromatography using HPLC and TLC as
1-(2,4-DICHLOROPHENYL)-2-(1H-IMIDAZOL-1-YL)ETHANOL (M6) and mandelic acid (M7).
The main radioactive fractions exceeding 10% of the applied radioactivity were M1 (unknown), M7 (mandelic acid) and M19 (unknown, purified water).
M1 reached maximum amounts of 45.6% and 44.7% of the applied radioactivity in marine water (day 3) and purified water (day 15), respectively. In marine water, it remained practically constant until the end of irradiation.
M7 increased steadily with study duration, representing a maximum amount of about 17% of the applied radioactivity from day 12 onwards in marine water and 10.5% of the applied radioactivity on day 15 in the purified water. The compounds M1 and M7 were therefore shown to be stable to photolysis.
M19 (unknown) was and additional major photodegradate, but in purified water only. After reaching a maximum of 14.8% on day 8, it decreased to 11.6% of the applied radioactivity by the end of the study (day 15).
Other minor photodegradates did not exceed 7.9% of the applied radioactivity in both test systems. M6 accounted for a maximum of 4.2% and 3.1% of the
applied radioactivity in marine (day 8) and purified (day 15) water, respectively.

The experimental Suntest photolytic half life (DT_{50}) was determined to be 1.1 days in marine water and 4.4 days in purified water. The corresponding environmental photolytic half lives (DT_{50}) were estimated to be about 3 days (marine water) or 12 days (purified water) natural summer sunlight at latitudes 30°N to 50°N.

Direct and indirect photo-degradation are therefore expected to contribute to
the elimination of miconazole nitrate in the environment.

However, as the calculated half lives are not relevant for Sweden (Sweden is located further north), the results of the ready biodegradation study are taken into account for the conclusion for the persistence criterium for miconazole nitrate.
Therefore, the following hazard sentence is applicable. Miconazole nitrate is potentially persistent

4. BIOACCUMULATION

Bioaccumulation and depuration of miconazole nitrate in the Rainbow trout (*Oncorhynchus mykiss*) was investigated in whole fish in a dynamic flow-through system according to OECD guideline No. 305. {9}
In the bioconcentration test with miconazole nitrate in Rainbow trout (*Oncorhynchus mykiss*) a BCF of 1949 was determined.
As the BCF ≥ 500, it can be concluded that miconazole nitrate has high potential for bioaccumulation.

6. REFERENCES

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