

## Aspirin®

M EF

**Bayer**

Tablett 500 mg

(Vita, runda, diameter 5 mm med prägling BAYER och ASPIRIN 0,5)

Analgetikum, antipyretikum och antiflogistikum

**Aktiv substans:**

Acetylsalicylsyra

**ATC-kod:**

N02BA01

Läkemedel från Bayer omfattas av Läkemedelsförsäkringen.

## Miljöpåverkan

### Acetylsalicylsyra

Miljörisk: Användning av acetylsalicylsyra har bedömts medföra låg risk för miljöpåverkan.

Nedbrytning: Acetylsalicylsyra bryts ned i miljön.

Bioackumulering: Acetylsalicylsyra har låg potential att bioackumuleras.

## Detaljerad miljöinformation

## Environmental Risk Classification

### Predicted Environmental Concentration (PEC)

PEC is calculated according to the following formula:

$$\text{PEC } (\mu\text{g/L}) = (A \cdot 10^9 \cdot (100 - R)) / (365 \cdot P \cdot V \cdot D \cdot 100) = 1.37 \cdot 10^{-6} \cdot A \cdot (100 - R)$$

$$\text{PEC} = 11 \mu\text{g/L}$$

Where:

**A = 80 016.0202 kg** (total sold amount API in Sweden year 2021, data from IQVIA/LIF).

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 =  $10 \cdot 10^6$

V (L/day) = volume of wastewater per capita and day = 200 (ECHA default (Reference 1))

D = factor for dilution of wastewater by surface water flow = 10 (ECHA default (Reference 1))

### Predicted No Effect Concentration (PNEC)

#### Ecotoxicological studies

*Algae* (green alga, *Desmodesmus subspicatus*):

NOEC/72 hours (growth rate) 14700 µg/L,

$E_r C_{50}$  72 hours (growth rate) >48 600 µg/L. Guideline OECD 201) (Reference 2)

*Crustacean* (waterflea *Daphnia magna*):

Chronic toxicity

NOEC 21 days (reproduction) ≥1000 µg/L. Guideline OECD 211) (Reference 3)

*Fish* (Zebrafish, *Danio rerio*)

Chronic toxicity

NOEC 30 days (growth) = 283 µg/L. Guideline OECD 210)

(Reference 4)

Other toxicity

NOEC 30 minutes (respiration inhibition) > 100 000 µg/L. Guideline OECD 209) (Reference 5)

The PNEC was calculated by division of the lowest effect level (NOEC) of the most sensitive taxonomic group considering an appropriate assessment factor (AF). The most sensitive taxonomic group were fish, and the lowest effect level was reported as NOEC = 283 µg/L. The regulatory default standard AF of 10 was used, which is applicable when there are chronic aquatic toxicity studies representing the three trophic levels (algae, crustaceans, and fish).  
$$\text{PNEC} = 283 \text{ µg/L} / 10 = 28.3 \text{ µg/L}$$

### **Environmental risk classification (PEC/PNEC ratio)**

The risk quotient PEC/PNEC was calculated with 11 µg/L / 28.3 µg/L = 0.39. Justification of chosen environmental phrase:

A risk quotient between 0.1 and 1 qualifies for the phrase "*Use of acetylsalicylic acid has been considered to result in low environmental risk.*"

### **Degradation**

#### **Biotic degradation**

*Ready degradability:*

Biodegradation of acetylsalicylic acid was assessed in a manometric respiration study. The test item concentration was 200 mg/L (ThOD). The study reported 69.6% biodegradation after 10 days and 83.3 % after 28 days, fulfilling the 10-day window criterion and is therefore considered readily biodegradable. Guideline OECD 301F (Reference 6)

Justification of the chosen degradation phrase: Acetylsalicylic acid is readily biodegradable, which qualifies for the phrase:  
*Acetylsalicylic acid is degraded in the environment.*

## Bioaccumulation

*Partitioning coefficient:*

A study on the n-octanol/water partition coefficient was conducted. The log  $D_{OW}$  reported with - 1.62 at pH 7 . Guideline OECD 107 (Reference 7)

Justification of chosen bioaccumulation phrase:

As the log  $D_{OW}$  was < 4 acetylsalicylic acid is not considered bioaccumulative which qualifies for the phrase *Acetylsalicylic acid has a low potential for bioaccumulation.*

## Excretion (metabolism)

In human body acetylsalicylic acid is deacetylated to salicylic acid and then further metabolized. It is predominantly excreted via urine as salicylic acid and subsequent salicylate metabolites salicyluric acid (glycine conjugate), salicyl phenolic glucuronide, salicyl acyl glucuronide, gentisic acid (oxidation product), gentisuric acid (glycine conjugate) and to a lesser extent in the unmetabolized form as parent compound (Reference 8). However, the acetylsalicylic acid metabolism in humans and therefore the proportions of the excreted urine metabolites significantly vary inter-individually depending on urine pH, sex, ethnicity, and variants in metabolizing enzymes (Reference 9).

## References

- (1) Guidance on information requirements and Chemical Safety Assessment Chapter R.16: Environmental exposure assessment. V3.0, Feb. 2016.
- (2) Growth inhibition test of BAY e4465 (Acetylsalicylic acid) with *Desmodesmus subspicatus*. Nonclinical Drug Safety, Bayer Schering AG, study no. T100981-9, report no. PH-38090
- (3) Reproduction study of BAY e4465 (Acetylsalicylic acid) in *Daphnia magna*. Nonclinical Drug Safety, Bayer Schering AG Study no. T100979-6, report no. PH-38263
- (4) ASS 180/840 KG Early-life-stage test with Zebrafish (*Danio rerio*) under Flow-Through Conditions). Nonclinical Drug Safety, Bayer Schering AG Study no. T100876-2, report no. R-9373
- (5) Respiration inhibition test with BAY e4465 (Acetylsalicylic acid) on activated sludge microorganisms. Nonclinical Drug Safety, Bayer Pharma AG, study no T101029-3, report no. PH-3898
- (6) Study on the biodegradability of BAY e4465 (Acetylsalicylic acid) in the manometric respiration test. Nonclinical Drug Safety, Bayer Schering Pharma AG, study no T101073-2, report no. PH-37791
- (7) BAY e 4465: Determination of the partition coefficient (n-octanol/water) by the shake-flask method at different pH values. Nonclinical Drug Safety, Bayer Pharma AG, study no T101857-2, report no. R-9744
- (8) Jjemba PK. Excretion and ecotoxicity of pharmaceutical and personal care products in the environment. *Ecotoxicology and Environmental Safety*, 2006; 63(1): 113-130.
- (9) Navarro SL, Saracino MR, Makar KW, Sushma TS, Li L, Zheng Y, Levy L, Schwarz Y, Bigler J, Potter JD, Lampe JW. Determinants of aspirin metabolism in healthy men and women: effects of dietary inducers of UDP-glucuronosyltransferases. *J Nutrigenet Nutrigenomics*, 2011; 4(2): 110-118.

