15 December 2022

Environmental Risk Assessment Data Summary

Active Pharmaceutical Ingredient	*Medical Product*
Cefuroxime	**Zinacef** **Zinnat**

Executive Summary

GSK is committed to ensuring that our compounds do not adversely affect the environment. We carry out state of the art environmental testing on our pharmaceuticals and use these data in risk assessments to evaluate potential for harm to the environment. We post summaries of our Environmental Risk Assessments on the GSK website as part of our commitment to data transparency.

This Environmental Risk Assessment (ERA) has been conducted for cefuroxime and demonstrates that the use of this drug substance is considered to result in insignificant environmental risk. This evaluation is based on the Predicted Environmental Concentration (PEC) to Predicted No Effects Concentration (PNEC) ratio of less than 0.1. Cefuroxime is an active ingredient in GSK pharmaceutical products and pharmaceutical products sold by other companies. This assessment takes account of the total quantity of active ingredient marketed by GSK and all other companies.

The following pages contain the technical background information.

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Technical Background Information

Environmental Fate

Cefuroxime is not readily biodegradable nor inherently biodegradable and has been shown to be chemically unstable in water. This substance is water soluble and a low partition coefficient suggests it is unlikely to bioconcentrate in exposed aquatic organisms. Significant removal from the aquatic environment is expected to occur in wastewater treatment plants via ultimate and primary biodegradation. It is not expected to persist in the environment. It is not likely to adsorb to sludge or biomass and is not expected to reach the terrestrial compartment to a significant extent.

PEC/PNEC Risk Quotient Calculation

The PEC/PNEC risk quotient calculation is the standard quantitative method of risk assessment and is approved by major national and international regulatory agencies [2, 3, 4].

Predicted Environmental Concentration (PEC)

The PEC has been calculated based on the following data:

$$\text{PEC } (\mu g/L) = \frac{A \times 1E+09 \times (100 - R)}{365 \times P \times V \times D \times 100}$$

where:

A (kg/year) = total use of Cefuroxime active based on sales (GSK + all other companies) in the European Union in 2021 (IQVIA Data).

R (%) = removal rate due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation. For Cefuroxime, removal has been based on biodegradation studies and removal from wastewater treatment plants, R = 86.80%.

P = Population of European Union + UK. Per capita use of drug substance A/P = 2.33E-04 kg/inhabitant (IQVIA Data).

V (L/day) = volume of wastewater per capita and day = 200, EMA default [2].

D = factor for dilution of wastewater by surface water flow = 10, EMA default [2].

PEC = 0.042 µg/L

Predicted No Effects Concentration (PNEC)

PNEC (µg/L) = EC10/10, where 10 is the assessment factor applied the lowest EC10 from blue-green algae (Cyanobacteria), which are usually very sensitive to antibiotics [5]. The EC10 for blue-green algae (11.70 µg/L) has been used for this calculation.

PNEC = 11.70/10 = 1.70 µg/L

PEC/PNEC Risk Characterisation

PEC/PNEC = 0.042/1.70

PEC/PNEC = 0.025

The PEC/PNEC is ≤ 0.1 which means the use of Cefuroxime is considered to result in insignificant environmental risk, in accordance with the fass environmental classification scheme [4].

All relevant environmental fate and ecotoxicity data are published in Section 12 of the Material Safety Data Sheet (MSDS) for the medical product. The MSDS is publicly available at http://www.msds-gsk.com/ExtMSDSlist.asp.

Metabolism and Excretion

Cefuroxime is not metabolised. After parenteral administration plasma levels decrease with a half-life of about 2 h. Cefuroxime is excreted unchanged into the urine by glomerular filtration; approximately 80 to 90 % of the dose is recovered in the urine within 24 h. Less than 1 % is excreted via the bile [1].

References

1. Summary of Product Characteristics Augmentin-Duo 625mg Tablets (Amoxicillin trihydrate). GlaxoSmithKline, May 2021. http://www.medicines.org.uk/EMC/
2. Committee for Medicinal Products for Human Use (CHMP); Guideline on the Environmental Risk Assessment of Medicinal Products for Human Use. 1 June 2006, Ref EMEA/CPMP/SWP/4447/00.

   https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-environmental-risk-assessment-medicinal-products-human-use-first-version_en.pdf

3. European Chemicals Agency (ECHA). 2008 Guidance on information requirements and chemical safety assessment. http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm

4. Fass Environmental Classification of Pharmaceuticals. 2012 v3.0 Guidance for Pharmaceutical Companies. www.fass.se

5. EMA Q&A for Environmental Risk Assessment. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/04/WC500105107.pdf