Environmental Risk Assessment Data Summary

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

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 all our pharmaceuticals and use these data in risk assessments to evaluate potential for harm to the environment. The results of these assessments suggest that no adverse environmental impact is likely to result from post-patient release of GSK pharmaceuticals into the environment.

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.

GlaxoSmithKline's public position statement on pharmaceuticals in the environment may be accessed via this link - ***GlaxoSmithKline's Position: Pharmaceuticals in the Environment****.*

The following pages contain the technical background information.

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

European Union

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

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 total sales (GSK + all other companies) in the European Union in 2013 (IMS Data). GSK accounted for 34% of this market in 2013.

R (%) = removal rate due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation. For cefuroxime it has been assumed that R = 0% as a worst case scenario [3].

P = number of inhabitants in the European Union (EU 27) = 500.151 x 10^6 (IMS Data).

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

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

NB: PEC, conservatively, is based on no metabolism and no removal of drug substance to sludge solids. It is assumed that 100% of drug substance enters the aquatic environment.

PEC = 0.047 µg/L

Predicted No Effects Concentration (PNEC)

PNEC (µg/L) = lowest EC50/1000, where 1000 is the assessment factor applied for three short-term EC50s. As all three EC50 are greater than (>) values the NOEC value for green alga (= 91,000 µg/L) has been used for this calculation since it is the most sensitive of the three tested species.

PNEC = 91,000/1,000 = 91.00 µg/L

PEC/PNEC Risk Characterisation

PEC/PNEC = 0.39/91

PEC/PNEC (European Union) = 0.0043

PEC/PNEC Risk Quotient Calculation

United States of America

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

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 total sales (GSK + all other companies) in the United States of America in 2013 (IMS Data). GSK accounted for 2% of this market in 2013.

R (%) = removal rate due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation. For cefuroxime it has been assumed that R = 0% as a worst case scenario [3].

P = number of inhabitants in the United States of America = 321.489 x 10^6 (IMS Data).

V (L/day) = volume of wastewater per capita and day = 370, USGS.

D = factor for dilution of waste water by surface water flow = 10, FDA default [5].

NB: PEC, conservatively, is based on no metabolism and no removal of drug substance to sludge solids. It is assumed that 100% of drug substance enters the aquatic environment.

PEC = 0.064 µg/L

Predicted No Effects Concentration (PNEC)

PNEC (µg/L) = lowest EC50/1000, where 1000 is the assessment factor applied for three short-term EC50s. As all three EC50 are greater than (>) values the NOEC value for green alga (= 91,000 µg/L) has been used for this calculation since it is the most sensitive of the three tested species.

PNEC = 91,000/1,000 = 91.00 µg/L

PEC/PNEC Risk Characterisation

PEC/PNEC = 0.064/91

PEC/PNEC (United States of America) = 0.00071

The PEC/PNEC is ≤ 0.1 which means the use of cefuroxime in the United States of America 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 Zinacef (Cefuroxime sodium). GlaxoSmithKline, March 2014. http://www.medicines.org.uk/EMC/
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