17 May 2022

Environmental Risk Assessment Data Summary

Active Pharmaceutical Ingredient	*Medical Product*
Atovaquone	**Malarone** **Wellvone**

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 atovaquone and a risk to the environment has not been excluded due to insufficient ecotoxicity data. Therefore, the Predicted Environmental Concentration (PEC) to Predicted No Effects Concentration (PNEC) ratio has not been calculated. Atovaquone 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

This substance has limited water solubility and is not likely to partition to air from water very readily. Atovaquone is lipophilic and does have potential for bioconcentration in exposed aquatic organisms. Atovaquone is not readily biodegradable or inherently biodegradable and therefore the fraction of this substance which partitions to the aquatic environment will persist. However, this substance likely to adsorb to sludge or biomass and is expected to reach the terrestrial compartment to a significant extent where it is predicted to sorb extensively to soil matrices. This substance is predicted to be rapidly biodegraded in soil.

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 Atovaquone based on patient consumption in the European Union and UK in 2020 (IQVIA Data).

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

P = Population of European Union + UK. Per capita use of drug substance A/P = 1.54E-05 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].

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 = 0.021 µg/L

Predicted No Effects Concentration (PNEC)

A PNEC may not be calculated because ecotoxicity data from all three trophic levels of aquatic organisms is not available.

PNEC = Not applicable

PEC/PNEC Risk Characterisation

PEC/PNEC = Not determined

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

In healthy volunteers there is no evidence that the drug is metabolised and there is negligible excretion of atovaquone in the urine, with parent drug being predominantly (>90%) excreted unchanged in faeces [1].

References

1. Summary of Product Characteristics Wellvone (Atovaquone) 750mg/5ml oral suspension. GlaxoSmithKline, November 2020. 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. http://www.emea.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500003978.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 Guidance for Pharmaceutical Companies. www.fass.se