15 December 2022

Environmental Risk Assessment Data Summary

Active Pharmaceutical Ingredient	*Medical Product*
Abacavir	**Kivexa** **Triumeq** **Trizivir** **Ziagen**

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 Abacavir 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. Abacavir 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

Abacavir is water soluble and is not likely to partition to air from water very readily. It is not readily nor inherently biodegradable. However, significant removal of the parent by primary degradation is expected at the STP and in water-sediment environs. This substance is not lipophilic and is unlikely to bioconcentrate in the tissues of aquatic species. A relatively low adsorption coefficient (Koc) suggests this material is unlikely to sorb to sludge to a significant extent. It will significantly partition to the aquatic environment where it will be slowly degraded (mineralized) over time.

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 Abacavir 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 Abacavir 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 = 6.34E-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 = 0.087 µg/L

Predicted No Effects Concentration (PNEC)

PNEC (µg/L) = lowest NOEC/10, where 10 is the assessment factor applied for three long-term NOECs. NOEC for water flea (= 5,600 ug/L) has been used for this calculation since it is the most sensitive of the three tested species.

PNEC = 5,600/10 = 560 µg/L

PEC/PNEC Risk Characterisation

PEC/PNEC = 0.087/560

PEC/PNEC = 0.00016

The PEC/PNEC is ≤ 0.1 which means the use of Abacavir 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

Abacavir is primarily metabolised by the liver with approximately 2% of the administered dose being renally excreted, as unchanged compound. The primary pathways of metabolism in man are by alcohol dehydrogenase and by glucuronidation to produce the 5'-carboxylic acid and 5'-glucuronide which account for about 66% of the administered dose. The metabolites are excreted in the urine. The mean half-life of abacavir is about 1.5 hours. Following multiple oral doses of abacavir 300 mg twice a day there is no significant accumulation of abacavir. Elimination of abacavir is via hepatic metabolism with subsequent excretion of metabolites primarily in the urine. The metabolites and unchanged abacavir account for about 83% of the administered abacavir dose in the urine. The remainder is eliminated in the faeces. [1].

References

1. Summary of Product Characteristics Ziagen (abacavir) 300mg tablets. GlaxoSmithKline, October 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