19 December 2022

Environmental Risk Assessment Data Summary

Active Pharmaceutical Ingredient	*Medical Product*
Naratriptan hydrochloride	**Naramig**

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 Naratriptan 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. Naratriptan 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 solubility in water and is not likely to partition to air from water very readily. Naratriptan is not readily nor inherently biodegradable and is expected to persist in the environment. Naratriptan is not lipophilic and has a low potential to bioconcentrate in exposed aquatic organisms. Moderate removal from the aquatic environment by sorption to sludge solids in wastewater treatment plants and surface water sediments is expected. It is likely to adsorb to sludge or biomass and is expected to reach the terrestrial compartment to a moderate 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 Naratriptan based on patient consumption in the European Union and UK in 2021 (IQVIA Data).

R (%) = removal rate due to loss by adsorption to sludge particles, by volatilization, hydrolysis or biodegradation. For Naratriptan 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 = 8.98E-08 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 = 0.00012 µg/L

Predicted No Effects Concentration (PNEC)

PNEC (µg/L) = lowest NOEC/1000, where 1000 is the assessment factor applied for three short-term NOECs. NOEC for fish (= 100,000 µg/L) has been used for this calculation since it is the most sensitive of the three tested species.

PNEC = 100,000/1,000 = 100 µg/L

PEC/PNEC Risk Characterisation

PEC/PNEC = 0.00012/100

PEC/PNEC = 0.0000072

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

Naratriptan is predominantly excreted in the urine with 50% of the dose recovered as unchanged naratriptan and 30% recovered as inactive metabolites. In vitro naratriptan was metabolised by a wide range of cytochrome P450 isoenzymes. Consequently significant metabolic drug interactions with naratriptan are not anticipated [1].

References

1. Summary of Product Characteristics Naramig (Naratriptan hydrochloride) tablets. 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