

## Environmental Risk Assessment Data Summary

<u>Active Pharmaceutical Ingredient</u>	<u>Medical Product</u>
Clobetasol propionate	Dermovate

### 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 Clobetasol propionate 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. Clobetasol propionate 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.**

## Technical Background Information

### Environmental Fate

Clobetasol propionate is not readily biodegradable nor inherently biodegradable and has limited solubility in water. It is expected to persist in the environment. A moderate partition coefficient suggests that clobetasol 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.

### 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:

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

where:

A (kg/year) = total use of Clobetasol propionate 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 Clobetasol propionate 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 = 8.53E-07 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 = 0.0012  $\mu\text{g/L}$**

## Predicted No Effects Concentration (PNEC)

PNEC ( $\mu\text{g/L}$ ) = lowest EC50/1000, where 1000 is the assessment factor applied for three acute EC50s. EC50 for fish (= 750  $\mu\text{g/L}$ ) has been used for this calculation since it is the most sensitive of the three tested species.

$$\text{PNEC} = 750/1000 = 0.75 \mu\text{g/L}$$

## PEC/PNEC Risk Characterisation

$$\text{PEC/PNEC} = 0.0012/0.75$$

$$\text{PEC/PNEC} = 0.0016$$

The PEC/PNEC is  $\leq 0.1$  which means the use of clobetasol is considered to result in insignificant environmental risk, in accordance with the pass 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

Following percutaneous absorption of clobetasol propionate, the drug probably follows the metabolic pathway of systemically administered corticosteroids, i.e. metabolised primarily by the liver and then excreted by the kidneys. However, systemic metabolism of clobetasol has never been fully characterised or quantified [1].

## References

1. Summary of Product Characteristics Dermovate cream (Clobetasol propionate). GlaxoSmithKline, March 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. [http://www.emea.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2009/10/WC500003978.pdf](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](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](http://www.fass.se)