MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and grant a waiver

MHRA-100105-PIP01-21

Scope of the Application

Active Substance(s)

ALPRAZOLAM

Condition(s)

Treatment of epileptic seizures

Pharmaceutical Form(s)

Inhalation powder

Route(s) of Administration

Inhalation use

Name / Corporate name of the PIP applicant

UCB Pharma Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, UCB Pharma Limited submitted to the licensing authority on 03/06/2021 13:59 BST an application for a Paediatric Investigation Plan

The procedure started on 20/06/2022 10:10 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to agree a paediatric investigation plan and grant a deferral and grant a waiver

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100105-PIP01-21

Of 07/07/2022 11:27 BST

On the adopted decision for ALPRAZOLAM (MHRA-100105-PIP01-21) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for ALPRAZOLAM, Inhalation powder , Inhalation use .

This decision is addressed to UCB Pharma Limited, 208 Bath Road, Slough, Berkshire, Slough, United Kingdom, SL1 3WE

ANNEX I

1. Waiver

1.1 Condition:

Treatment of epileptic seizures The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 12 years of age Pharmaceutical form(s): Inhalation powder Route(s) of administration: Inhalation use Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of epileptic seizures

2.2 Indication(s) targeted by the PIP:

Rapid cessation of seizures in patients with stereotypical prolonged seizures from 12 years to less than 18 years of age.

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from 12 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Inhalation powder

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable
Non-Clinical Studies	0	Not applicable
Clinical Studies	3	Study 1 (UP0100) Open label, uncontrolled trial to evaluate the pharmacokinetics (PK), safety, and tolerability of alprazolam for inhalation use in adolescent from 12 years to less than 18 years of age with an established diagnosis of focal, generalised, or focal and generalised epilepsy, and to contribute to modelling of the PK. Study 2 (EP0162) Double-blind, randomised, placebo-controlled, study to evaluate the efficacy and safety of alprazolam for inhalation use in adolescents from 12 years to less than 18 years of age (and adults) with epilepsy with stereotypical prolonged seizures, to demonstrate superiority over placebo and contribute to modelling of the PK/PD. Study 3 (EPO165) Open label, uncontrolled extension study to evaluate safety, tolerability, and activity of alprazolam for inhalational use in adolescents from12 years to less than 18 years of age (and adults) with stereotypical prolonged seizures.
Extrapolation, Modeling & Simulation Studies	2	Study 4 (CL0498 Part 2) Modelling and simulation population pharmacokinetic (PK) study to confirm the dose of alprazolam for inhalation use in the treatment of

		prolonged stereotypical seizures in adolescents from 12 years to less than 18 years of age. Study 5 (M1) Modelling and simulation population pharmacokinetic/ pharmacodynamic (PK/PD) study to confirm that the dosing of alprazolam for inhalation use in adolescent study participants and to identify exposure - response relationships.
Other Studies	0	Not applicable
Other Measures	0	Not applicable

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	28/02/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes