EMA/515863/2023

European Medicines Agency decision

P/0499/2023

of 1 December 2023

on the acceptance of a modification of an agreed paediatric investigation plan for alprazolam, (EMEA-003043-PIP01-21-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0220/2022 issued on 10 June 2022,

Having regard to the application submitted by UCB Pharma S.A. on 29 June 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 13 October 2023, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for alprazolam, inhalation powder, inhalation use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to UCB Pharma S.A., Allee de la Recherche, 60, 1070 - Brussels, Belgium.

EMA/PDCO/316103/2023
Amsterdam, 13 October 2023

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-003043-PIP01-21-M01

Scope of the application

Active substance(s):

Alprazolam

Invented name and authorisation status:

See Annex II

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 S.A.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, UCB Pharma S.A. submitted to the European Medicines Agency on 29 June 2023 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0220/2022 issued on 10 June 2022.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 14 August 2023.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:
    - to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion.
2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of epileptic seizures

The waiver applies to:

- the paediatric population from birth to less than 12 years of age;
- inhalation powder, inhalation use;
- 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:

Treatment of epileptic seizures

2.1.1. Indication(s) targeted by the PIP

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

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 12 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Inhalation powder

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable.
Non-clinical studies	Not applicable.
Clinical studies	**Study 1 (UP0100)** Open-label, uncontrolled trial to evaluate pharmacokinetics (PK), safety and tolerability of alprazolam for inhalation use in adolescents from 12 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 safety and efficacy of alprazolam for inhalation use in adolescents from 12 to less than 18 years of age (and adults) with epilepsy with

	stereotypical prolonged seizures to demonstrate superiority over placebo. **Study 3 (EP0165)** Open-label, uncontrolled extension study to evaluate safety, tolerability and activity of alprazolam for inhalation use in adolescents from 12 to less than 18 years of age (and adults) with stereotypical prolonged seizures.
Extrapolation, modelling and simulation studies	**Study 4 (CL0498 (part 2))** Modelling and simulation population pharmacokinetic (PK) study to confirm the dose of the alprazolam for inhalation use in the treatment of prolonged stereotypical seizures in adolescents from 12 to less than 18 years of age. **Study 5 (M1)** Modelling and simulation population pharmacokinetic (PK) study to support dosing recommendation of alprazolam for inhalation use in adolescents from 12 to less than 18 years of age for treatment of prolonged stereotypical seizures by matching exposure between adolescent and adult patients with epilepsy.
Other studies	Not applicable.
Other measures	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By December 2026.
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.