EMA/441673/2024

European Medicines Agency decision

P/0350/2024

of 27 September 2024

on the acceptance of a modification of an agreed paediatric investigation plan for ganaxolone (Ztalmy), (EMEA-002341-PIP01-18-M03) 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/0361/2019 issued on 4 November 2019, the decision P/0171/2021 issued on 9 April 2021 and the decision P/0404/2021 issued on 1 October 2021,

Having regard to the application submitted by Marinus Pharmaceuticals Inc. on 3 June 2024 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 6 September 2024, 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 ganaxolone (Ztalmy), oral suspension, age-appropriate oral liquid formulation, oral 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 Marinus Pharmaceuticals Inc., 5 Radnor Corporate Center 100 Matsonford Rd, Suite 500, PA 19087 – Radnor, United States.

EMA/PDCO/279472/2024
Amsterdam, 6 September 2024

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

EMEA-002341-PIP01-18-M03

Scope of the application

Active substance(s):

Ganaxolone

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of cyclin-dependent kinase-like 5 deficiency disorder

Pharmaceutical form(s):

Oral suspension

Age-appropriate oral liquid formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Marinus Pharmaceuticals Inc.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Marinus Pharmaceuticals Inc. submitted to the European Medicines Agency on 3 June 2024 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/0361/2019 issued on 4 November 2019, the decision P/0171/2021 issued on 9 April 2021 and the decision P/0404/2021 issued on 1 October 2021.

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

The procedure started on 8 July 2024.

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.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

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 cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- oral suspension, age-appropriate oral liquid formulation, oral 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 cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder

2.1.1. Indication(s) targeted by the PIP

Adjunctive treatment of seizures in paediatric patients aged 6 months to < 18 years old with CDKL5 deficiency disorder who did not respond satisfactorily to previous treatment

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

From 6 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Oral suspension

Age-appropriate oral liquid formulation

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of a sodium benzoate-free ganaxolone oral suspension (50 mg/mL) appropriate for the paediatric population in the age range from 6 months to less than 18 years. **Study 2** Study deleted in EMEA-002341-PIP01-18-M03.
Non-clinical studies	Not applicable

Clinical studies	**Study 3** Double-blind, randomised, placebo-controlled add-on efficacy trial followed by a long-term open-label phase of adjunctive ganaxolone treatment for the treatment of primary-type seizures in paediatric patients (and young adults) with genetically confirmed cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) from 2 to less than 18 years of age (1042-CDD-3001). **Study 4** Double-blind, randomised, placebo-controlled add-on efficacy trial of adjunctive ganaxolone treatment for the treatment of primary-type seizures in paediatric patients with genetically confirmed cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) from 6 months to less than 2 years of age (1042-CDD-3002).
Extrapolation, modelling and simulation studies	**Study 5** Paediatric population pharmacokinetic (PK/PD) study to enable modelling of the effect of intrinsic and extrinsic factors on the PK and pharmacodynamics of ganaxolone in the paediatric patients from 6 months to less than 18 years.
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:	Yes
Date of completion of the paediatric investigation plan:	By September 2028
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:

Condition(s) and authorised indication(s)

Treatment of epilepsy

Authorised indication(s):

- ZTALMY is indicated for the adjunctive treatment of epileptic seizures associated with cyclindependent kinase-like 5 (CDKL5) deficiency disorder (CDD) in patients 2 to 17 years of age. ZTALMY may be continued in patients 18 years of age and older
  - Invented name(s): ZTALMY
  - Authorised pharmaceutical form(s): Oral suspension
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure