EMA/197408/2021

European Medicines Agency decision

P/0171/2021

of 9 April 2021

on the acceptance of a modification of an agreed paediatric investigation plan for ganaxolone ,(EMEA-002341-PIP01-18-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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary 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,

Having regard to the application submitted by Marinus Pharmaceuticals Inc. on 18 December 2020 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 26 March 2021, in accordance with Article 22 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation,

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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for ganaxolone, 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/26613/2021
Amsterdam, 26 March 2021

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

EMEA-002341-PIP01-18-M01

Scope of the application

Active substance(s):

Ganaxolone

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 18 December 2020 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 application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 26 January 2021.

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 Norwegian Paediatric Committee member 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 annex 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	Number of measures	Description
Quality-related studies	2	**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** Single-arm open label study to assess the palatability of benzoate - free ganaxolone suspension 50 mg/mL in healthy adult subjects (with no ingestion).
Non-clinical	0	Not applicable.

studies		
Clinical studies	2	**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	1	**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	0	Not applicable.
Other measures	0	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 March 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes