EMA/251788/2024

European Medicines Agency decision

P/0188/2024

of 14 June 2024

on the agreement of a paediatric investigation plan and on the granting of a waiver for trofinetide (EMEA-003587-PIP01-24) 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 application submitted by Acadia Pharmaceuticals Inc. on 23 January 2024 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 26 April 2024, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 13 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 agreement of a paediatric investigation plan and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a waiver.

[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

A paediatric investigation plan for trofinetide, oral solution, oral use, gastroenteral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A waiver for trofinetide, oral solution, oral use, gastroenteral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to Acadia Pharmaceuticals Inc., 12830 El Camino Real, Suite 400, 92130 - San Diego, United States.

EMA/PDCO/127506/2024
Amsterdam, 26 April 2024

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a waiver

EMEA-003587-PIP01-24

Scope of the application

Active substance(s):

Trofinetide

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of Rett syndrome

Pharmaceutical form(s):

Oral solution

Route(s) of administration:

Oral use

Gastroenteral use

Name/corporate name of the PIP applicant:

Acadia Pharmaceuticals Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Acadia Pharmaceuticals Inc. submitted for agreement to the European Medicines Agency on 23 January 2024 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 26 February 2024.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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

2. The measures and timelines of the agreed 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 Rett syndrome

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- oral solution, oral use, gastrointestinal 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 Rett syndrome

2.1.1. Indication(s) targeted by the PIP

Treatment of Rett syndrome (RTT)

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

From 2 years to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Oral solution

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable
Non-clinical studies	**Study 1** Repeat-dose oral dosage study in juvenile rats to evaluate the toxicity, and toxicokinetic profile and reversibility of possible toxicity or effects on development of trofinetide (0621-16031). **Study 2** Repeat-dose oral dosage study in juvenile dogs to evaluate the toxicity, and toxicokinetic profile and reversibility of possible toxicity or effects on development of trofinetide (0621-16032).

Clinical studies	**Study 3** Randomised, double-blind, placebo-controlled, dose-escalation study of trofinetide in female paediatric patients from 16 to less than 18 years of age (and adult females) with RTT.(Neu-2566-RETT-001). **Study 4** Randomised, double-blind, placebo-controlled, parallel group, dose-ranging study of the safety, pharmacokinetics and efficacy of trofinetide in female paediatric patients aged from 5 to less than 16 years diagnosed with post-regression, classic Rett syndrome. (Neu-2566-RETT-002). **Study 5** Randomised, double-blind, placebo-controlled, parallel group study to evaluate efficacy, safety and pharmacokinetics of trofinetide in female subjects aged from 5 to less than 18 years diagnosed with post-regression, classic Rett syndrome. (ACP-2566-003)**.** **Study 6** 40-week open-label extension study to evaluate the long-term safety, tolerability, efficacy, and pharmacokinetics of trofinetide in paediatric and adult patients with RTT who completed PIP Study 5 (ACP-2566-003). (ACP-2566-004) **Study 7** 32-month, multicentre, open-label extension study to evaluate long-term safety and tolerability of trofinetide in paediatric and adult patients with RTT who completed PIP Study 6 study (Study ACP-2566-004). (ACP-2566-005) **Study 8** Open-label study to evaluate safety and tolerability, pharmacokinetics, and efficacy of trofinetide in female paediatric subjects aged 2 to less than 5 years with Rett syndrome. (ACP-2566-009)
Modelling and simulation analyses	**Study 9** Population pharmacokinetic model to establish the dose of trofinetide to be used in paediatric patients and exposure-response (E-R) model to confirm appropriateness of target exposure and support extrapolation of efficacy in patients below 5 years of age (ACP-2566-MS-007, ACP-2566-MS-008, ACP-2566-MS-010, ACP-2566-MS-009).
Other studies	Not applicable
Extrapolation plan	Efficacy in paediatric population age 2 to less than 5 years to be extrapolated from efficacy established paediatric

	population from 5 years to less than 18 years (Study 5) supported by PK and safety assessments from Study 8 and 9.

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 June 2023
Deferral for one or more measures contained in the paediatric investigation plan:	No

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.