EMA/929775/2022

European Medicines Agency decision

P/0529/2022

of 30 December 2022

on the acceptance of a modification of an agreed paediatric investigation plan for linaclotide (Constella), (EMEA-000927-PIP01-10-M07) 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/110/2011 issued on 6 May 2011, the decision P/0106/2013 issued on 30 April 2013, the decision P/0252/2016 issued on 26 September 2016, the decision P/0135/2020 issued, on 15 April 2020 and the decision P/0216/2021 issued on 8 June 2021,

Having regard to the application submitted by AbbVie Deutschland GmbH & Co. KG on 4 August 2022 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 11 November 2022, 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.

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

[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 linaclotide (Constella), capsule, hard, oral use, 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 AbbVie Deutschland GmbH & Co KG, Knollstraβe, 67061 - Ludwigshafen, Germany.

EMA/PDCO/695155/2022
Amsterdam, 11 November 2022

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

EMEA-000927-PIP01-10-M07

Scope of the application

Active substance(s):

Linaclotide

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of functional constipation

Pharmaceutical form(s):

Capsule, hard

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

AbbVie Deutschland GmbH & Co. KG

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, AbbVie Deutschland GmbH & Co. KG submitted to the European Medicines Agency on 4 August 2022 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/110/2011 issued on 6 May 2011, the decision P/0106/2013 issued on 30 April 2013, the decision P/0252/2016 issued on 26 September 2016, the decision P/0135/2020 issued on 15 April 2020 and the decision P/0216/2021 issued on 8 June 2021.

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

The procedure started on 12 September 2022.

Scope of the modification

Some measures 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 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 functional constipation

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- capsule, hard, oral use;
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of functional constipation

2.1.1. Indication(s) targeted by the PIP

Treatment of functional constipation

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)

Capsule, hard

2.1.4. Measures

Area	Description
Quality-related sutdies	**Study 1** Development of capsules for "sprinkles" mode of administration.
Non-clinical studies	**Study 2** A 9-Week Oral Gavage Toxicity Study in Juvenile mice. (MNP-103-054)
Clinical studies	**Study 3** Randomised, double-blind, placebo-controlled, dose-ranging study of Linaclotide in children, aged from 6 years to less than 18 years, with functional constipation (LIN-MD-62) **Study 4** Randomised, double-blind, placebo-controlled, ascending-dose, dose-ranging study of Linaclotide in children, aged from 2 years to less than 6 years, with functional constipation (LIN-MD-67)

	Study 5 Two-part study with an open ascending, multidose dose-finding part (Part 1) to assess the safety of linaclotide, and a randomised, double-blind, placebo-controlled part (Part 2) to evaluate the safety and efficacy of linaclotide in children from 6 months to less than 2 years of age with functional constipation. (M21-862) **Study 6** Randomised, double-blind, placebo-controlled, parallel-group, confirmatory study of Linaclotide in children aged from 6 years to less than 18 years with functional constipation. (LIN-MD-64) **Study 7** Randomised, double-blind, placebo-controlled, parallel-group, confirmatory study of Linaclotide in children aged from 2 years to less than 6 years with functional constipation with an open label 24-week on-treatment extension. (M21-572) **Study 8** Open label, long-term safety study of Linaclotide in children aged from 6 years to less than 18 years with functional constipation. (LIN-MD-66) **Study 9** Randomised, double-blind, parallel-group, safety, and efficacy study, of linaclotide versus placebo in children, aged from 6 months to less than 2 years, with functional constipation with a 24 week open-label on treatment extension.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By December 2027
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)

1. Treatment of irritable bowel syndrome

Authorised indication(s): Constella is indicated for the symptomatic treatment of moderate to severe irritable bowel syndrome with constipation (IBS-C) in adults.

- Invented name(s): Constella
- Authorised pharmaceutical form(s): capsule, hard
- Authorised route(s) of administration: oral use
- Authorised via centralised procedure