EMA/557955/2016

European Medicines Agency decision

P/0252/2016

of 26 September 2016

on the acceptance of a modification of an agreed paediatric investigation plan for linaclotide (Constella), (EMEA-000927-PIP01-10-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 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/110/2011 issued on 6 May 2011 and the decision P/0106/2013 issued on 30 April 2013,

Having regard to the application submitted by Allergan Pharmaceuticals International Limited on 28 April 2016 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 16 September 2016, 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, following a re-examination procedure of the Paediatric Committee's opinion according to Article 25(3) Regulation (EC) No 1901/2006, 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 linaclotide (Constella), capsule, hard, 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 Allergan Pharmaceuticals International Limited, Clonshaugh Industrial Estate, Coolock, 17 – Dublin, Ireland.

EMA/PDCO/584989/2016
London, 16 September 2016

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

EMEA-000927-PIP01-10-M03

Scope of the application

Active substance(s):

Linaclotide

Invented name:

Constella

Condition(s):

Treatment of functional constipation

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Capsule, hard

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Allergan Pharmaceuticals International Limited

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Allergan Pharmaceuticals International Limited submitted to the European Medicines Agency on 28 April 2016 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 and the decision P/0106/2013 issued on 30 April 2013.

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

An Opinion was adopted by the Paediatric Committee on 22 July 2016 for the above mentioned product. Allergan Pharmaceuticals International Limited received the Paediatric Committee Opinion on 1 August 2016.

On 31 August 2016 Allergan Pharmaceuticals International Limited submitted to the European Medicines Agency a written request including detailed grounds for a re-examination of the Opinion.

The re-examination procedure started on 1 September 2016.

Scope of the modification

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

Final Opinion

1. The Paediatric Committee, having assessed the detailed grounds for re-examination, in accordance with Article 25(3) of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

1.1. to revise its opinion and

- to agree to the changes regarding the measures and the timelines of the paediatric investigation plan and the timelines of the deferral in the scope set out in the Annex I of this opinion;

1.2. following re-examination, to amend the scope of the modifications of the paediatric investigation plan.

The Norwegian Paediatric Committee member 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 functional constipation

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- for capsule, hard, for 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, for oral use

2.1.4. Measures

Area	Number of measures	Description
Quality	1	Measure 1 Development of capsules for “sprinkles” mode of administration.
Non-clinical	1	Measure 2 A 9-Week Oral Gavage Toxicity Study in Juvenile mice.
Clinical	7	Measure 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 Measure 4 Randomised, double-blind, placebo-controlled, ascending-dose, dose-ranging study of Linaclotide in children, aged from 3 years to less than 6 years, with Functional Constipation Measure 5 Randomised, double-blind, placebo-controlled, ascending-dose, dose-ranging study of Linaclotide in children, aged from 6 months to less than 3 years, with Functional Constipation. Measure 6 Randomised, double-blind, placebo-controlled, parallel-group, confirmatory study of Linaclotide in children aged from 3 years to less than 18 years with Functional Constipation. Measure 7 Randomised, double-blind, placebo-controlled, parallel-group, confirmatory study of Linaclotide in children aged from 6 months to less than 3 years with Functional Constipation. Measure 8 Open label, long-term safety study of Linaclotide in children aged from 3 years to less than 18 years with Functional Constipation. Measure 9 Open label, long-term safety study of Linaclotide in children aged from 6 months to less than 3 years with Functional Constipation.

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

Condition(s) and authorised indication(s):

Symptomatic treatment of moderate to severe irritable bowel syndrome with constipation (IBS-C) in adults

Authorised pharmaceutical form(s):

Hard capsule

Authorised route(s) of administration:

Oral use