EMA/792977/2017

European Medicines Agency decision

P/0387/2017

of 19 December 2017

on the acceptance of a modification of an agreed paediatric investigation plan for bezlotoxumab (Zinplava), (EMEA-001645-PIP01-14-M02) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

European Medicines Agency decision

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on the acceptance of a modification of an agreed paediatric investigation plan for bezlotoxumab (Zinplava), (EMEA-001645-PIP01-14-M02) in accordance with Regulation (EC) No 1901/2006 of the 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/0340/2014 issued on 22 December 2014,

Having regard to the application submitted by Merck Sharp & Dohme (Europe), Inc. on 21 August 2017 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 10 November 2017, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for bezlotoxumab (Zinplava), concentrate for solution for infusion, intravenous 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 Merck Sharp & Dohme (Europe), Inc., Clos du Lynx, 5, B-1200 – Brussels, Belgium.

EMA/PDCO/573640/2017
London, 10 November 2017

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

EMEA-001645-PIP01-14-M02

Scope of the application

Active substance(s):

Bezlotoxumab

Invented name:

Zinplava

Condition(s):

Treatment of *Clostridium difficile* infection

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Merck Sharp & Dohme (Europe), Inc.

Information about the authorised medicinal product:

See Annex II

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Merck Sharp & Dohme (Europe), Inc. submitted to the European Medicines Agency on 21 August 2017 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0340/2014 issued on 22 December 2014.

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

The procedure started on 12 September 2017.

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 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

Not applicable

2. Paediatric investigation plan

2.1. Condition

Treatment of *Clostridium difficile* infection

2.1.1. Indication(s) targeted by the PIP

Prevention of recurrence of *Clostridium difficile* infection related diarrhoea in adults and paediatric patients

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Concentrate for solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1:** Development of a vial containing max. 25 ml of 25 mg/ml concentrate for solution for infusion of bezlotoxumab.
Non-clinical studies	0	Not applicable
Clinical studies	2	**Study 2:** Randomised, double-blind, single dose, placebo controlled trial to evaluate safety, efficacy, and pharmacokinetics of bezlotoxumab as add-on to standard of care antibiotic treatment in children from 1 to less than 18 years of age with *Clostridium difficile* infection (CDI). **Study 3:** Open label, single dose trial to evaluate safety, tolerability, and pharmacokinetics of bezlotoxumab in children from birth to less than 2 years of age with suspected or documented *Clostridium difficile* Infection (CDI), or at risk for developing CDI.
Extrapolation, modelling and simulation studies	2	**Study 4:** Modelling and simulation study to evaluate the use of *bezlotoxumab* in children from birth to less than 18 years of age with *Clostridium difficile* Infection (CDI).

		Study 5: Analysis of existing adult PK data and data collected from paediatric studies with bezlotoxumab to inform paediatric dose recommendations assuming that the PK/PD relationship is similar between adults and children.
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:	No
Date of completion of the paediatric investigation plan:	By November 2024
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):

1. Treatment of *Clostridium difficile* infection (CDI)

Authorised indication(s):

- Prevention of recurrence of *Clostridium difficile* infection (CDI) in adults at high risk for recurrence of CDI.

Authorised pharmaceutical form(s):

Concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous use