EMA/100904/2020

European Medicines Agency decision

P/0104/2020

of 20 March 2020

on the acceptance of a modification of an agreed paediatric investigation plan for bezlotoxumab (Zinplava), (EMEA-001645-PIP01-14-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/0340/2014 issued on 22 December 2014 and the decision P/0387/2017 issued on 19 December 2017,

Having regard to the application submitted by Merck Sharp & Dohme (Europe), Inc. on 28 October 2019 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and proposing a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 31 January 2020, in accordance with Article 22 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 acceptance of changes to the agreed paediatric investigation plan and to the deferral and on the granting of a waiver.

(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.

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

[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

A waiver for bezlotoxumab (Zinplava), concentrate for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to Merck Sharp & Dohme (Europe), Inc., Clos du Lynx, 5, 1200 - Brussels, Belgium.

EMA/PDCO/601062/2019
Amsterdam, 31 January 2020

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

EMEA-001645-PIP01-14-M03

Scope of the application

Active substance(s):

Bezlotoxumab

Invented name:

Zinplava

Condition(s):

Prevention of recurrence of *Clostridioides 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

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 28 October 2019 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 and the decision P/0387/2017 issued on 19 December 2017.

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

The procedure started on 3 December 2019.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. A waiver for a new paediatric subset has been added.

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;
   - to grant a waiver for one or more subsets of the paediatric population concluded in accordance with Article 11(1)(c) of Regulation (EC) No 1901/2006 as amended, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   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 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:

Prevention of recurrence of *Clostridioides difficile* infection

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- concentrate for solution for infusion, intravenous use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition

Prevention of recurrence of *Clostridioides difficile* infection

2.1.1. Indication(s) targeted by the PIP

Prevention of recurrence of *Clostridioides difficile* infection (CDI) in paediatric patients at high risk for recurrence of CDI.

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

From 1 year 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	1	**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 *Clostridioides difficile* infection (CDI).

		[Study 3 was deleted as a result of procedure EMEA-001645-PIP01-14-M03]
Extrapolation, modelling and simulation studies	2	**Study 4:** Modelling and simulation study to evaluate the use of bezlotoxumab in children from 1 to less than 18 years of age with *Clostridioides difficile* Infection (CDI). **Study 5:** Extrapolation study to support the use of bezlotoxumab in children from 1 year to less than 18 years of age who are at high risk of developing CDI recurrence.
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 2022
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. Prevention of recurrence of *Clostridioides difficile* infection

Authorised indication(s):

- Prevention of recurrence of *Clostridioides 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