EMA/166789/2017

European Medicines Agency decision

P/0104/2017

of 11 April 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral for entolimod (EMEA-002020-PIP01-16) 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 application submitted by Cleveland Biolabs, Inc. on 8 August 2016 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 24 February 2017, in accordance with Article 18 of Regulation (EC) No 1901/2006 and Article 21 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 deferral.

(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 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

A paediatric investigation plan for entolimod, solution for injection, intramuscular 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 deferral for entolimod, solution for injection, intramuscular 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 Cleveland BioLabs Inc, 73 High Street, 14203 - Buffalo, NY, USA.

EMA/PDCO/2397/2017
London, 24 February 2017

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

EMEA-002020-PIP01-16

Scope of the application

Active substance(s):

Entolimod

Condition(s):

Treatment of acute radiation syndrome

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Intramuscular use

Name/corporate name of the PIP applicant:

Cleveland Biolabs, Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Cleveland Biolabs, Inc. submitted for agreement to the European Medicines Agency on 8 August 2016 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 13 September 2016.

Supplementary information was provided by the applicant on 12 December 2016. The applicant proposed modifications to the paediatric investigation plan.

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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 18 of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

   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 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 annex 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 acute radiation syndrome

2.1.1. Indication(s) targeted by the PIP

Entolimod is indicated for reducing the risk of death following exposure to potentially lethal irradiation.

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)

Solution for injection

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1:** Development of an age-appropriate solution for injection
Non-clinical studies	6	**Study 2:** Randomised, blinded, placebo-controlled study of dose-dependent effects of entolimod on survival and biomarker induction in rhesus macaques (*Macaca mulatta*) after lethal irradiation (CBL1.1-N-01-Rs-23) **Study 3:** Randomized, open-label, placebo-controlled, pharmacokinetic and pharmacodynamic study of multiple entolimod dose levels in non-irradiated rhesus macaques (*Macaca mulatta*) (CB5BD-P-Rs-001) **Study 4:** Ex vivo pilot pharmacodynamic study of entolimod in blood samples from neonatal, infant, toddler and adult human donors (CB5GP-P-IV-002P) **Study 5:** Ex vivo pharmacodynamic study of entolimod in blood samples from neonatal, infant, toddler and adult human donors (CB5GP-P-IV-002) **Study 6:** Ex vivo pharmacodynamic study of entolimod in blood samples from neonatal, infant, toddler and adult rhesus macaques (*Macaca mulatta*) (CB5GP-P-IV-003)

		Study 7: Randomised, blinded, pharmacodynamic, pharmacokinetic, and safety study of entolimod in neonatal and infant/toddler rhesus macaques (*Macaca mulatta*) (CB5BD-P-Rs-003)
Clinical studies	0	Not applicable.
Extrapolation, modelling and simulation studies	2	**Study 8:** Modelling and simulation study to support dose conversion from rhesus macaques (*Macaca mulatta*) to adults, adolescents and children from 2 years of age. **Study 9:** Modelling and simulation study to support dose conversion from rhesus macaques (*Macaca mulatta*) to neonates, infants and toddlers.
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:	Yes
Date of completion of the paediatric investigation plan:	By January 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes