EMA/630131/2017

European Medicines Agency decision

P/0295/2017

of 29 September 2017

on the acceptance of a modification of an agreed paediatric investigation plan for entolimod (EMEA-002020-PIP01-16-M01) 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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on the acceptance of a modification of an agreed paediatric investigation plan for entolimod (EMEA-002020-PIP01-16-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/0104/2017 issued on 11 April 2017,

Having regard to the application submitted by Cleveland Biolabs, Inc. on 18 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 15 September 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.

(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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for entolimod, solution for injection, intramuscular 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 Cleveland Biolabs, Inc., 73 High Street, 14203 - Buffalo, New York, United States.

EMA/PDCO/546183/2017
London, 15 September 2017

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

EMEA-002020-PIP01-16-M01

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 22 of Regulation (EC) No 1901/2006 as amended, Cleveland Biolabs, Inc. submitted to the European Medicines Agency on 18 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/0104/2017 issued on 11 April 2017.

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

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 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 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