EMA/538560/2018

European Medicines Agency decision

P/0290/2018

of 12 September 2018

on the acceptance of a modification of an agreed paediatric investigation plan for autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human ATP-binding cassette, subfamily D, member 1 (ABCD1) cDNA (EMEA-001244-PIP01-11-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

P/0290/2018

of 12 September 2018

on the acceptance of a modification of an agreed paediatric investigation plan for autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human ATP-binding cassette, subfamily D, member 1 (ABCD1) cDNA (EMEA-001244-PIP01-11-M02) 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/0119/2013 issued on 3 May 2013 and the decision P/0329/2016 issued on 2 December 2016,

Having regard to the application submitted by bluebird bio France on 7 May 2018 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 27 July 2018, 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 autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human ATP-binding cassette, subfamily D, member 1 (ABCD1) cDNA, dispersion for infusion, intravenous 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 bluebird bio France, 155 rue du Faubourg Saint-Denis, 75010 – Paris, France.

EMA/PDCO/301394/2018
London, 27 July 2018

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

EMEA-001244-PIP01-11-M02

Scope of the application

Active substance(s):

Autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human ATP-binding cassette, subfamily D, member 1 (ABCD1) cDNA

Condition(s):

Treatment of adrenoleukodystrophy

Pharmaceutical form(s):

Dispersion for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

bluebird bio France

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, bluebird bio France submitted to the European Medicines Agency on 7 May 2018 an application for modification of the agreed paediatric investigation plan as set out in the European Medicines Agency's decision P/0119/2013 issued on 3 May 2013 and the decision P/0329/2016 issued on 2 December 2016.

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

The procedure started on 29 May 2018.

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 adrenoleukodystrophy

2.1.1. Indication(s) targeted by the PIP

Treatment of adrenoleukodystrophy

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)

Dispersion for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality	0	Not applicable.
Non-clinical	4	**Study 1 (NC-12-001)** In vitro pharmacology, Evaluation of adrenoleukodystrophy protein (ALDP) expression level in primary ALDP negative fibroblast **Study 2 (NC-12-051)** In vitro pharmacology, Demonstration of efficient transduction on one cells lot of AMN CD34+ cells using Lenti-D Lentiviral Vector (LVV) by measuring vector copy number (VCN), ALDP expression, and very long chain fatty acids (VLCFA) reduction **Study 3 (NC-12-058)** In vitro pharmacology, Demonstration of efficient transduction with Lenti-D LVV of three CD34+ cell lots derived from healthy donor and AMN CD34+ cells, including the assessment of the frequency of Long Term Culture–Initiating Cells (LTC-IC) present in the AMN CD34+ cell population **Study 4 (B1-13-003)** Investigation of biodistribution of cells derived from Lenti-D transduced cells into the brain

Clinical	1	**Study 5 (ALD-102)** Open label, single dose study in boys with cerebral adrenoleukodystrophy (CALD) to demonstrate the activity and safety of Lenti-D modified autologous haematopoietic stem cells in the treatment of CALD

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By May 2019
Deferral for one or more studies contained in the paediatric investigation plan:	No