EMA/762335/2018

European Medicines Agency decision

P/0400/2018

of 26 November 2018

on the acceptance of a modification of an agreed paediatric investigation plan for autologous CD34+ hematopoietic stem cells transduced *ex vivo* with EFS lentiviral vector encoding for the human adenosine deaminase gene (EMEA-001974-PIP01-16-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/0400/2018

of 26 November 2018

on the acceptance of a modification of an agreed paediatric investigation plan for autologous CD34+ hematopoietic stem cells transduced *ex vivo* with EFS lentiviral vector encoding for the human adenosine deaminase gene (EMEA-001974-PIP01-16-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/0077/2017 issued on 17 March 2017, and the decision P/0331/2017 issued on 31 October 2017,

Having regard to the application submitted by Orchard Therapeutics Limited on 16 July 2018 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a waiver and proposing a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 November 2018, in accordance with Article 22 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, following a re-examination procedure of the Paediatric Committee's opinion according to Article 25(3) Regulation (EC) No 1901/2006, an opinion on the acceptance of changes to the agreed paediatric investigation plan and on the granting of a deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision on the granting of 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

Changes to the agreed paediatric investigation plan for autologous CD34+ hematopoietic stem cells transduced *ex vivo* with EFS lentiviral vector encoding for the human adenosine deaminase gene, 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

A deferral for autologous CD34+ hematopoietic stem cells transduced *ex vivo* with EFS lentiviral vector encoding for the human adenosine deaminase gene, dispersion 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 Orchard Therapeutics Limited, 108 Cannon Street, EC4N 6EU - London, United Kingdom.

EMA/PDCO/781411/2018 Corr
London, 16 November 2018

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

EMEA-001974-PIP01-16-M02

Scope of the application

Active substance(s):

Autologous CD34+ hematopoietic stem cells transduced *ex vivo* with EFS lentiviral vector encoding for the human adenosine deaminase gene

Condition(s):

Treatment of severe combined immunodeficiency due to adenosine deaminase deficiency

Pharmaceutical form(s):

Dispersion for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Orchard Therapeutics Limited

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
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, Orchard Therapeutics Limited submitted to the European Medicines Agency on 16 July 2018 an application for modification of the agreed paediatric investigation plan with a waiver as set out in the European Medicines Agency's decision P/0077/2017 issued on 17 March 2017, and the decision P/0331/2017 issued on 31 October 2017.

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

An Opinion was adopted by the Paediatric Committee on 19 October 2018 for the above mentioned product. Orchard Therapeutics Limited received the Paediatric Committee Opinion on 29 October 2018.

On 2 November 2018 Orchard Therapeutics Limited submitted to the European Medicines Agency a written request including detailed grounds for a re-examination of the Opinion.

The re-examination procedure started on 3 November 2018.

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified and a deferral granted.

Final Opinion

1. The Paediatric Committee, having assessed the detailed grounds for re-examination, in accordance with Article 25(3) of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

1.1. to revise its opinion and

- to agree to the changes regarding the measures of the paediatric investigation plan in the scope set out in the Annex I of this opinion;
- to grant a deferral.

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 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 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

1.1. Condition

Treatment of severe combined immunodeficiency due to adenosine deaminase deficiency

The waiver applies to:

- the paediatric population from birth to less than 1 month;
- dispersion for infusion, intravenous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition

Treatment of severe combined immunodeficiency due to adenosine deaminase deficiency

2.1.1. Indication(s) targeted by the PIP

Treatment of patients diagnosed with adenosine deaminase deficient severe combined immunodeficiency (ADA-SCID)

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

From 1 month 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-related studies	1	**Study 1** Development of a cryopreserved dispersion for infusion formulation.
Non-clinical studies	0	Not applicable.
Clinical studies	3	**Study 2** Open-label, non-randomised, single-centre, historically controlled trial to evaluate safety and efficacy of autologous CD34+ hematopoietic stem cells transduced *ex vivo* with EFS lentiviral vector encoding for the human adenosine deaminase gene in children from 1 month to less than 18 years of age with adenosine deaminase deficiency severe combined immunodeficiency (ADA-SCID).

		Study 3 Open-label, non-randomised, historically controlled trial to evaluate safety and efficacy of autologous CD34+ hematopoietic stem cells transduced *ex vivo* with EFS lentiviral vector encoding for the human adenosine deaminase gene in children from 1 month to less than 18 years of age with adenosine deaminase deficiency severe combined immunodeficiency (ADA-SCID). **Study 4** Open-label, non-randomised, single centre, uncontrolled trial to evaluate activity (overall survival and event-free survival) and safety of a cryopreserved formulation of autologous CD34+ hematopoietic stem cells transduced *ex vivo* with EFS lentiviral vector encoding for the human adenosine deaminase gene in children from 1 month to less than 18 years of age with adenosine deaminase deficiency severe combined immunodeficiency (ADA-SCID). **Study 5** *(added in procedure EMEA-001974-PIP01-16-M01 and removed in procedure EMEA-001974-PIP01-16-M02)*
Extrapolation, modelling and simulation studies	0	Not applicable.
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 2021
Deferral for one or more measures contained in the paediatric investigation plan:	Yes