EMA/205922/2015

European Medicines Agency decision

P/0103/2015

of 11 May 2015

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 (CTL019) (EMEA-001654-PIP01-14) 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

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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 Novartis Europharm Limited on 4 July 2014 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 20 March 2015, in accordance with Article 18 of Regulation (EC) No 1901/2006, and of its own motion in accordance with Article 21 of said Regulation, 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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(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.

(4) 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

A paediatric investigation plan for autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 (CTL019), cell suspension for infusion, intravenous 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 autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 (CTL019), cell suspension for infusion, intravenous 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

A waiver for autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 (CTL019), cell suspension for infusion, intravenous 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 4

This decision is addressed to Novartis Europharm Limited, Frimley Business Park, GU16 7SR – Camberley, United Kingdom.

Done at London, 11 May 2015

For the European Medicines Agency
Jordi Llinares Garcia
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/1205/2015 Corr
London, 20 March 2015

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

EMEA-001654-PIP01-14

Scope of the application

Active substance(s):

Autologous T cells transduced with lentiviral vector containing a chimeric antigen receptor directed against CD19 (CTL019)

Condition(s):

Treatment of B lymphoblastic leukaemia/lymphoma

Pharmaceutical form(s):

Cell suspension for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Novartis Europharm Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted for agreement to the European Medicines Agency on 4 July 2014 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 13 August 2014.

Supplementary information was provided by the applicant on 17 December 2014. 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 on its own motion in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Icelandic and the Norwegian Paediatric Committee members agree 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 B lymphoblastic leukaemia/lymphoma

The waiver applies to:

- the paediatric population weighing less than 6 kg;
- cell suspension 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 B lymphoblastic leukaemia/lymphoma

2.1.1. Indication(s) targeted by the PIP

Treatment of CD19+ B cell acute lymphoblastic leukaemia (ALL) in paediatric patients whose disease is refractory to a standard chemotherapy regimen, relapsed after stem cell transplantation (SCT) or are ineligible for allogenic SCT.

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

Less than 18 years of age and weighing at least 6 kg

2.1.3. Pharmaceutical form(s)

Cell suspension for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.

Area	Number of measures	Description
Clinical studies	4	**Study 1** Open-label, single-arm, posology-finding study to evaluate safety and feasibility of administration of redirected autologous T cells engineered to contain anti-CD19 attached to TCRzeta and 4-1BB signalling domains (CAR-19 cells) in patients from 1 year to less than 18 years of age (and adults) with a chemotherapy-resistant or refractory CD19+ leukaemia or lymphoma. **Study 2** Open-label, single-arm, single-dose study to evaluate safety and activity of CTL019 in patients from 2 to less than 18 years of age at the time of initial diagnosis (and adults) with CD19+ B-cell acute lymphoblastic leukaemia/CD19+ B cell lymphoblastic lymphoma whose disease is refractory to a standard chemotherapy regimen, relapsed after stem cell transplantation (SCT) or are otherwise ineligible for allogeneic SCT. **Study 3** Open-label, single-arm, single-dose study to evaluate safety and activity of CTL019 in patients from 3 to less than 18 years of age (and adults) with CD19+ B cell acute lymphoblastic leukaemia (ALL) whose disease is refractory to a standard chemotherapy regimen, relapsed after stem cell transplantation (SCT) or are otherwise ineligible for allogeneic SCT. **Study 4** Open-label, two-cohort study to evaluate manufacturing and safety of CTL019 in children less than 3 years of age and weighing at least 6 kg with CD19+ B cell acute lymphoblastic leukaemia (ALL)/CD19+ B cell lymphoblastic lymphoma at high risk for relapse and at relapse/refractory stage.
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 December 2021
Deferral for one or more measures contained in the paediatric investigation plan:	Yes