EMA/626321/2017

European Medicines Agency decision

P/0287/2017

of 4 October 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for autologous CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor (JCAR017), (EMEA-001995-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.

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 Celgene Europe Limited on 28 November 2016 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 18 August 2017, in accordance with Article 18 of Regulation (EC) No 1901/2006 and 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 CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor (JCAR017), dispersion 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 CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor (JCAR017), dispersion 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 CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor (JCAR017), dispersion 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 Celgene Europe Limited, 1 Longwalk road, Stockley Park, UB11 1DB – Uxbridge, United Kingdom.

EMA/PDCO/378370/2017
London, 18 August 2017

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

EMEA-001995-PIP01-16

Scope of the application

Active substance(s):

Autologous CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor (JCAR017)

Condition(s):

Treatment of B-lymphoblastic leukaemia/lymphoma

Treatment of mature B-cell neoplasms

Pharmaceutical form(s):

Dispersion for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Celgene Europe Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Celgene Europe Limited submitted for agreement to the European Medicines Agency on 28 November 2016 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 3 January 2017.

Supplementary information was provided by the applicant on 26 May 2017. The applicant proposed modifications to the paediatric investigation plan.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

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;
   - 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 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 B-lymphoblastic leukaemia/lymphoma

The waiver applies to:

- the paediatric population weighing less than 6 kg;
- 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.

1.2. Condition:

Treatment of mature B-cell neoplasms

The waiver applies to:

- the paediatric population weighing less than 6 kg;
- dispersion for infusion, intravenous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies 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 paediatric patients with CD19+ relapsed or refractory B-cell acute lymphoblastic leukaemia

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)

Dispersion for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	Study 1 Development of a new manufacturing process and formulation to generate JCAR017 product for paediatric patients (and young adults)
Non-clinical studies	0	Not applicable
Clinical studies	2	Study 2 Open-label, single dose, single-arm, three-cohort, two-parts trial to evaluate the activity and safety of JCAR017 in children less than 18 years of age and weighing at least 6 kg with relapsed or refractory (r/r) B-cell acute lymphoblastic leukaemia (B-ALL) or with r/r B-cell non-Hodgkin's lymphoma (B-NHL) Study 3 Open-label, non-randomised, multi-cohort trial to assess the safety, feasibility, and efficacy of administering a T cell product containing CD4 and CD8 cells derived from patient peripheral blood mononuclear cells that has been genetically modified using a self-inactivating lentiviral vector to express a CD19-specific chimeric antigen receptor (CAR) and the marker EGFRt (truncated epidermal growth factor receptor) to children from 1 year to less than 18 years of age (and adults) weighing at least 10 kg with relapsed or refractory CD19+ leukaemia
Extrapolation, modelling and simulation studies	0	Not applicable
Other studies	0	Not applicable
Other measures	0	Not applicable

2.2. Condition:

Treatment of mature B-cell neoplasms

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with CD19+ relapsed or refractory diffuse-large B-cell lymphoma, Burkitt lymphoma or primary mediastinal large B-cell lymphoma

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

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

2.2.3. Pharmaceutical form(s)

Dispersion for infusion

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	1	Study 1 Development of a new manufacturing process and formulation to generate JCAR017 product for paediatric patients (and young adults) (same measure as for 'Treatment of B-lymphoblastic leukaemia/lymphoma')
Non-clinical studies	0	Not applicable
Clinical studies	2	Study 2 Open-label, single dose, single-arm, three-cohort, two-parts trial to evaluate the activity and safety of JCAR017 in children less than 18 years of age and weighing at least 6 kg with relapsed or refractory (r/r) B-cell acute lymphoblastic leukaemia (B-ALL) or with r/r B-cell non-Hodgkin's lymphoma (B-NHL) (same measure as for 'Treatment of B-lymphoblastic leukaemia/lymphoma') Study 3 Open-label, non-randomised, multi-cohort trial to assess the safety, feasibility, and efficacy of administering a T cell product containing CD4 and CD8 cells derived from patient peripheral blood mononuclear cells that has been genetically modified using a self-inactivating lentiviral vector to express a CD19-specific chimeric antigen receptor (CAR) and the EGFRt (truncated epidermal growth factor receptor) to children from 1 year to less than 18 years of age (and adults) weighing at least 10 kg with relapsed or refractory CD19+ leukaemia (same measure as for 'Treatment of B-lymphoblastic leukaemia/lymphoma')
Extrapolation, modelling and simulation studies	0	Not applicable

Area	Number of measures	Description
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 August 2022
Deferral for one or more measures contained in the paediatric investigation plan:	Yes