EMA/640003/2008

European Medicines Agency decision

P/0198/2019

of 12 June 2019

on the acceptance of a modification of an agreed paediatric investigation plan for autologous CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor (JCAR017) (EMEA-001995-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.

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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 European Medicines Agency's decision P/0287/2017 issued on 4 October 2017 and the decision P/0119/2018 on 11 April 2018,

Having regard to the application submitted by Celgene Europe B.V. on 18 January 2019 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 26 April 2019, 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 and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the 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 CD4+ and CD8+ T cells expressing a CD19-specific chimeric antigen receptor (JCAR017), dispersion for infusion, intravenous use, including changes to the deferral, 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 Celgene Europe B.V., Winthontlaan 6 N, 3526 KV – Utrecht, The Netherlands.

EMA/PDCO/101609/2019
Amsterdam, 26 April 2019

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

EMEA-001995-PIP01-16-M02

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 B.V.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Celgene Europe B.V. submitted to the European Medicines Agency on 18 January 2019 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0287/2017 issued on 4 October 2017 and the decision P/0119/2018 on 11 April 2018.

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

The procedure started on 26 February 2019.

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 and to the deferral 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 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, multi-cohort trial to evaluate the activity and safety of JCAR017 in children less than 18 years of age (and adults) 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, multi-cohort trial to evaluate the activity and safety of JCAR017 in children less than 18 years of age (and adults) 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
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 November 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes