

EMA/190160/2019

European Medicines Agency decision

P/0149/2019

of 17 April 2019

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 lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains (bb2121) (EMEA-002369-PIP01-18) 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 726/2004¹,

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 Agency²,

Having regard to the application submitted by Celgene Europe B.V. on 21 May 2018 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 1 March 2019, in accordance with Article 17 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 T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains (bb2121), 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 T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains (bb2121), 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 T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains (bb2121), 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 B.V., Winthontlaan 6N, 3526 KV - Utrecht, The Netherlands.

EMA/PDCO/834130/2018

London, 1 March 2019

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

EMA-002369-PIP01-18

Scope of the application

Active substance(s):

Autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains (bb2121)

Condition(s):

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 16(1) of Regulation (EC) No 1901/2006 as amended, Celgene Europe B.V. submitted for agreement to the European Medicines Agency on 21 May 2018 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 26 June 2018.

Supplementary information was provided by the applicant on 21 November 2018. The applicant proposed modifications to the paediatric investigation plan.

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 17(1) 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 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(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition:

Treatment of mature B-cell neoplasms

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with relapsed or refractory BCMA+ B-cell non-Hodgkin lymphoma

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 (bb2121-CMC-001) Development of a new formulation to generate autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains (bb2121) product for paediatric patients.
Non-clinical studies	2	Study 2 (bb2121-NC-001) Development of a validated immunohistochemistry (IHC) assay that can be used to detect surface expression of B-cell maturation antigen (BCMA) protein in biopsies obtained from paediatric patients with B-cell non-Hodgkin lymphoma (NHL).

		Study 3 (bb2121-NC-002) Quantification of the intensity of validated immunohistochemistry (IHC) staining in biopsy samples obtained from paediatric patients with B NHL to provide target validation support for a clinical study with bb2121 in patients with B-NHL.
Clinical studies	1	Study 4 (bb2121-BCM-001) Open-label trial to evaluate pharmacokinetics, safety and activity, of bb2121 in children less than 18 years of age and weighing at least 6 kg with relapsed/refractory (r/r), BCMA-positive, B-NHL.
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 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes