EMA/366055/2022

European Medicines Agency decision

P/0215/2022

of 10 June 2022

on the acceptance of a modification of an agreed paediatric investigation plan for tisagenlecleucel (Kymriah), (EMEA-001654-PIP01-14-M04) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0103/2015 issued on 11 May 2015, the decision P/0337/2016 issued on 2 December 2016, the decision P/0270/2017 issued on 22 September 2017 and the decision P/0008/2019 issued on 3 January 2019,

Having regard to the application submitted by Novartis Europharm Limited on 24 January 2022 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 22 April 2022, 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.

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

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for tisagenlecleucel (Kymriah), 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

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0266/2017 issued on 4 September 2017, including subsequent modifications thereof.

Article 3

This decision is addressed to Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, 4 – Dublin, Ireland.

EMA/PDCO/53310/2022
Amsterdam, 22 April 2022

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

EMEA-001654-PIP01-14-M04

Scope of the application

Active substance(s):

Tisagenlecleucel

Invented name:

Kymriah

Condition(s):

Treatment of B cell acute lymphoblastic leukaemia / lymphoblastic lymphoma

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Dispersion for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Novartis Europharm Limited

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted to the European Medicines Agency on 24 January 2022 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/0103/2015 issued on 11 May 2015, the decision P/0337/2016 issued on 2 December 2016, the decision P/0270/2017 issued on 22 September 2017 and the decision P/0008/2019 issued on 3 January 2019.

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

The procedure started on 21 February 2022.

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified.

Opinion

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 in the scope set out in the Annex I of this opinion.

The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

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 annexes 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 cell acute lymphoblastic leukaemia/lymphoblastic 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.

2. Paediatric investigation plan

2.1. Condition

Treatment of B cell acute lymphoblastic leukaemia/lymphoblastic 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)

Dispersion for infusion

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable.
Non-clinical studies	Not applicable.
Clinical studies	**Study 1 (CHP959)** 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 (14BT022/CCTL019B2205J) Open-label, single-arm, single-dose study to evaluate safety and activity of tisagenlecleucel in patients from 3 to less than 18 years of age (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 (CCTL019B2202)** Open-label, single-arm, single-dose study to evaluate safety and activity of tisagenlecleucel 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 (CCTL019B210X)** *(deleted in procedure EMEA-001654-PIP01-14-M03)* **Study 5 (CCTL019G2201J)** *(added in procedure EMEA-001654-PIP01-14-M03)* Open-label, single-arm study to evaluate the efficacy and safety of tisagenlecleucel in de novo high-risk paediatric patients from 1 year to less than 18 years of age (and adults) with B-cell acute lymphoblastic leukemia (B-ALL) who have positive minimal residual disease at the end of consolidation therapy.
Extrapolation, modelling and simulation studies	Not applicable.
Other measures	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 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of B cell acute lymphoblastic leukaemia/lymphoblastic lymphoma

Authorised indication(s):

- Treatment of paediatric and young adult patients up to 25 years of age with B-cell acute lymphoblastic leukaemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse

2. Treatment of mature B-cell neoplasms

Authorised indication(s):

Treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy

Authorised pharmaceutical form(s):

Dispersion for infusion

Authorised route(s) of administration:

Intravenous use