

EMA/418665/2021

European Medicines Agency decision P/0321/2021

of 11 August 2021

on the agreement of a paediatric investigation plan and on the granting of a deferral for allogeneic anti-CD19 CAR T cells produced using CRISPR/Cas9 to disrupt the T cell receptor alpha constant (TRAC) and β 2-microglobulin (B2M) genomic loci and a recombinant adeno-associated viral vector to deliver donor template for insertion of the anti-CD19 CAR expression cassette into the TRAC locus (CTX110), (EMEA-002881-PIP01-20) 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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on the agreement of a paediatric investigation plan and on the granting of a deferral for allogeneic anti-CD19 CAR T cells produced using CRISPR/Cas9 to disrupt the T cell receptor alpha constant (TRAC) and β 2-microglobulin (B2M) genomic loci and a recombinant adeno-associated viral vector to deliver donor template for insertion of the anti-CD19 CAR expression cassette into the TRAC locus (CTX110), (EMA-002881-PIP01-20) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 CRISPR Therapeutics AG on 9 September 2020 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 25 June 2021, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 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.
- (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.

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 allogeneic anti-CD19 CAR T cells produced using CRISPR/Cas9 to disrupt the T cell receptor alpha constant (TRAC) and β 2-microglobulin (B2M) genomic loci and a recombinant adeno-associated viral vector to deliver donor template for insertion of the anti-CD19 CAR expression cassette into the TRAC locus (CTX110), dispersion for injection, 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 allogeneic anti-CD19 CAR T cells produced using CRISPR/Cas9 to disrupt the T cell receptor alpha constant (TRAC) and β 2-microglobulin (B2M) genomic loci and a recombinant adeno-associated viral vector to deliver donor template for insertion of the anti-CD19 CAR expression cassette into the TRAC locus (CTX110), dispersion for injection, 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

This decision is addressed to CRISPR Therapeutics AG, Baarerstrasse 14, CH6300 – Zug, Switzerland.

EMA/PDCO/198019/2021
Amsterdam, 25 June 2021

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

EMA-002881-PIP01-20

Scope of the application

Active substance(s):

Allogeneic anti-CD19 CAR T cells produced using CRISPR/Cas9 to disrupt the T cell receptor alpha constant (TRAC) and β 2-microglobulin (B2M) genomic loci and a recombinant adeno-associated viral vector to deliver donor template for insertion of the anti-CD19 CAR expression cassette into the TRAC locus (CTX110)

Condition(s):

Treatment of B-lymphoblastic leukaemia/lymphoma

Treatment of mature B cell neoplasms

Pharmaceutical form(s):

Dispersion for injection

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

CRISPR Therapeutics AG

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, CRISPR Therapeutics AG submitted for agreement to the European Medicines Agency on 9 September 2020 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 13 October 2020.

Supplementary information was provided by the applicant on 16 March 2021. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a waiver.

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.

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

2. The measures and timelines of the agreed paediatric investigation plan 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

Not applicable

2. Paediatric investigation plan

2.1. Condition:

Treatment of B-lymphoblastic leukaemia/lymphoma

2.1.1. Indication(s) targeted by the PIP

Treatment of relapsed/refractory B cell acute lymphoblastic leukaemia

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Dispersion for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable
Non-clinical studies	0	Not applicable
Clinical studies	1	Study 1 Open-label, historically controlled trial in two parts to evaluate pharmacokinetics, safety, activity and immunogenicity of allogeneic anti-CD19 CAR T cells produced using CRISPR/Cas9 to disrupt the T cell receptor alpha constant (TRAC) and β 2-microglobulin (B2M) genomic loci and a recombinant adeno-associated viral vector to deliver donor template for insertion of the anti-CD19 CAR expression cassette into the TRAC locus (CTX110) in children from birth to less than 18 years of age with relapsed/refractory B cell acute lymphoblastic leukaemia (ALL) or with relapsed/refractory B cell non-Hodgkin lymphoma (NHL)
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 relapsed/refractory B cell non-Hodgkin lymphoma

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

From birth to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Dispersion for infusion

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable
Non-clinical studies	0	Not applicable
Clinical studies	1	Study 1 Same as for condition 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 March 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes