

EMA/579392/2022

European Medicines Agency decision P/0253/2022

of 8 July 2022

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for autologous tumour-infiltrating lymphocytes (TILs) isolated from a patient's cancer tissue and expanded *ex vivo* (ITIL-168) (EMEA-003072-PIP01-21) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency²,

Having regard to the application submitted by Instil Bio, Inc. on 12 July 2021 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 20 May 2022, 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, as amended.

² OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for autologous tumour-infiltrating lymphocytes (TILs) isolated from a patient's cancer tissue and expanded *ex vivo* (ITIL-168), 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 tumour-infiltrating lymphocytes (TILs) isolated from a patient's cancer tissue and expanded *ex vivo* (ITIL-168), 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 tumour-infiltrating lymphocytes (TILs) isolated from a patient's cancer tissue and expanded *ex vivo* (ITIL-168), 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 Instil Bio, Inc., 3963 Maple Avenue, #350, 75219 - Dallas, United States.

EMA/PDCO/120199/2022
Amsterdam, 20 May 2022

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

EMA-003072-PIP01-21

Scope of the application

Active substance(s):

Autologous tumour-infiltrating lymphocytes (TILs) isolated from a patient's cancer tissue and expanded *ex vivo* (ITIL-168)

Condition(s):

Treatment of melanoma

Pharmaceutical form(s):

Dispersion for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Instil Bio, Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Instil Bio, Inc. submitted for agreement to the European Medicines Agency on 12 July 2021 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 17 August 2021.

Supplementary information was provided by the applicant on 4 February 2022. 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)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population.

The Paediatric Committee member of Norway 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 melanoma

The waiver applies to:

- the paediatric population from birth to less than 12 years of age;
- dispersion for infusion, intravenous use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of melanoma

2.1.1. Indication(s) targeted by the PIP

Treatment of adolescent patients from 12 years to less than 18 years of age with persistent advanced melanoma following treatment with at least 1 prior line of systemic therapy.

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

From 12 years to less than 18 years of age

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 (ITIL-168-101 (DELTA-1)) Open-label, uncontrolled, multicentre study to evaluate the safety and activity of autologous tumour-infiltrating lymphocytes (TILs) isolated from a patient's cancer tissue and expanded ex vivo (ITIL-168) in adolescents from 12 years to less than 18 years of age (and adults) with persistent advanced melanoma following treatment with at least 1 prior line of systemic therapy.

Extrapolation, modelling and simulation studies	Study 2 Study using a Bayesian hierarchical model with commensurate prior to evaluate the safety and efficacy of ITIL-168 in adolescent subjects from 12 years to less than 18 years of age with persistent advanced melanoma following treatment with at least 1 prior line of systemic therapy. Data from paediatric and adult patients from Study 1 (ITIL-168-101 (DELTA-1)) will be used.
Other 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:	No
Date of completion of the paediatric investigation plan:	By March 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes