EMA/282173/2023

European Medicines Agency decision

P/0275/2023

of 14 July 2023

on the acceptance of a modification of an agreed paediatric investigation plan for talimogene laherparepvec (Imlygic), (EMEA-001251-PIP01-11-M06) 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 acceptance of a modification of an agreed paediatric investigation plan for talimogene laherparepvec (Imlygic), (EMEA-001251-PIP01-11-M06) in accordance with Regulation (EC) No 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/0047/2013 issued on 1 March 2013, the decision P/0105/2016 issued on 15 April 2016 and the decision P/0353/2016 issued on 9 December 2016, the decision P/0087/2017 issued on 24 March 2017, the decision P/0187/2020 issued on 13 May 2020 and the decision P/0005/2022 issued on 31 January 2022,

Having regard to the application submitted by Amgen Europe B.V. on 2 February 2023 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 May 2023, 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 talimogene laherparepvec (Imlygic), solution for injection, intralesional 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 is addressed to Amgen Europe B.V., Minervum 7061, 4817-ZK - Breda, The Netherlands.

EMA/PDCO/96245/2023 Corr. [1]
Amsterdam, 26 May 2023

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

EMEA-001251-PIP01-11-M06

Scope of the application

Active substance(s):

Talimogene laherparepvec

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of melanoma

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Intralesional use

Name/corporate name of the PIP applicant:

Amgen Europe B.V.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Amgen Europe B.V. submitted to the European Medicines Agency on 2 February 2023 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/0047/2013 issued on 1 March 2013, the decision P/0105/2016 issued on 15 April 2016 and the decision P/0353/2016 issued on 9 December 2016, the decision P/0087/2017 issued on 24 March 2017, the decision P/0187/2020 issued on 13 May 2020 and the decision P/0005/2022 issued on 31 January 2022.

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

[1] 27 June 2023

The procedure started on 27 March 2023.

Scope of the modification

Some 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 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.

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 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 melanoma

The waiver applies to:

- the paediatric population from birth to less than 2 years;
- solution for injection, intralesional use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of 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 with unresectable stage IIIB/C/IVM1a melanoma

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

From 2 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable
Non-clinical studies	**Study 1** Paediatric tumour cell cytotoxicity study **Study 2** Paediatric tumour model xenograft study
Clinical studies	**Study 3** Multi-centre, open-label, dose de-escalation study to evaluate the tolerability, safety and activity of talimogene laherparepvec in patients from 2 years of age with melanoma or with an advanced non-CNS tumours that are amenable to direct injection and for which no effective treatment is known (20110261)

	Study 4 *deleted in EMEA-001251-PIP01-11-M05*
Extrapolation, modelling and simulation studies	**Study 5** *added in EMEA-001251-PIP01-11-M04* Exposure response analysis from the existing adult data in Study 20120324 and comparison to the exposure data in Study 3 (20110261) to support the inference that similar lesion level exposure of talimogene laherparepvec, at which efficacy was observed in adult melanoma, can be achieved in adolescent melanoma lesions **Study 6** *added in EMEA-001251-PIP01-11-M04* Efficacy analysis of the young adult melanoma subgroup (from 18 to less than 36 years of age) from 4 talimogene laherparepvec monotherapy studies using Bayesian extrapolation with data collected from the older adult melanoma subgroup (from 36 years of age and older) to support extrapolation of efficacy from adult patients with advanced melanoma to adolescent patients with advanced melanoma
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:	Yes
Date of completion of the paediatric investigation plan:	By October 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of melanoma

Authorised indication(s):

- Treatment of adults with unresectable melanoma that is regionally or distantly metastatic (Stage IIIB, IIIC and IVM1a) with no bone, brain, lung or other visceral disease.
  - Invented name(s): Imlygic
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Intralesional use.
  - Authorised via centralised procedure.