MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept of change(s) to the agreed paediatric investigation plan and to the deferral.

MHRA-100442-PIP01-22-M01

Scope of the Application

Active Substance(s)

TALIMOGENE LAHERPAREPVEC

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 Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Amgen Limited submitted to the licensing authority on 23/02/2022 11:34 GMT an application for a

The procedure started on 31/10/2022 13:58 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral.

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100442-PIP01-22-M01

Of 22/11/2022 08:48 GMT

On the adopted decision for TALIMOGENE LAHERPAREPVEC (MHRA-100442-PIP01-22-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan).

This decision applies to a for TALIMOGENE LAHERPAREPVEC, Solution for injection , Intratumoral use .

This decision is addressed to Amgen Limited, 216 Cambridge Science Park, Milton Road, Cambridge, Cambridge, United Kingdom, CB4 0WA

ANNEX I

1. Waiver

1.1 Condition:

Treatment of melanoma The waiver applies/applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years. Pharmaceutical form(s): Solution for injection Route(s) of administration: Intralesional use Reason for granting waiver: 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(s):

Treatment of melanoma.

2.2 Indication(s) targeted by the PIP:

Treatment of adolescent patients with unresectable stage IIIB/C/IVM1a melanoma.

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

From 2 years to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Solution for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	2	Study 1 Paediatric tumour cell cytotoxicity study. Study 2 Paediatric tumour model xenograft study.
Clinical Studies	1	Study 3 (20110261) 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 advanced non-CNS tumours that are amenable to direct injection and for which no effective treatment is known. Study 4 Deleted in MHRA-100442-PIP01-22-M01.
Extrapolation, Modeling & Simulation Studies	2	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	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	YES
Date of completion of the paediatric investigation plan:	31/10/2023
Deferral of one or more studies contained in the paediatric investigation plan:	YES