MHRA
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Canary Wharf
London
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United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

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

MHRA-101352-PIP01-24-M01

Scope of the Application

Active Substance(s)

Autologous tumour-infiltrating lymphocytes (LN-144/LN-145)

Condition(s)

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms)

Pharmaceutical Form(s)

Dispersion of infusion

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Iovance Biotherapeutics, Inc.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Iovance Biotherapeutics, Inc. submitted to the licensing authority on 26/02/2024 16:14 GMT an application for a Modification

The procedure started on 27/02/2024 14:06 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-101352-PIP01-24-M01

Of 17/04/2024 16:51 BST

On the adopted decision for Autologous tumour-infiltrating lymphocytes (LN-144/LN-145) (MHRA-101352-PIP01-24-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 Modification for Autologous tumour-infiltrating lymphocytes (LN-144/ LN-145), Dispersion of infusion , INTRAVENOUS USE .

This decision is addressed to Iovance Biotherapeutics, Inc., 825 Industrial Road, Suite 400, San Carlos, UNITED STATES OF AMERICA, 94070

ANNEX I

1. Waiver

1.1 Condition:

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms) The waiver applies / applied to: Paediatric Subset(s): The paediatric population weighing less than 8 kg Pharmaceutical form(s): Dispersion of infusion Route(s) of administration: INTRAVENOUS USE Reason for granting waiver: 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(s):

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms)

2.2 Indication(s) targeted by the PIP:

Treatment of solid malignant neoplasms in children and adolescents with relapsed or refractory solid tumours for which no effective therapy is known.

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

The paediatric population weighing at least 8 kg and less than 18 years of age

2.4 Pharmaceutical Form(s):

Dispersion of infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	1	Study 1 (TP-19-028) In vitro study to assess the feasibility of producing tumour infiltrating lymphocytes (TIL) from paediatric tumour samples using the same process used to manufacture TIL products from tumour tissue from adults to characterise the phenotype of paediatric TILs.
Clinical Studies	2	Study 2 (IOV-PED-101) Multi-centre, open-label, single-arm study to evaluate the safety and tolerability and anti-tumour activity of autologous tumour-infiltrating lymphocytes (LN-144/LN-145) in paediatric patients from 8 kg of body weight and less than 18 years of age (and adults) with a relapsed or refractory solid malignant tumour for which no effective therapy is available. Study 3 (IOV-PED-201) Multi-centre, open-label, single-arm study to evaluate the safety and tolerability and anti-tumour activity of autologous tumour-infiltrating lymphocytes (LN-144/LN-145) in paediatric patients from 8 kg of body

		weight and less than 18 years of age (and adults) with a solid malignant tumour selected based on the results of study IOV-PED-101.
Extrapolation, Modeling & Simulation Studies	0	Not applicable.
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:	No
Date of completion of the paediatric investigation plan:	31/01/2031
Deferral of one or more studies contained in the paediatric investigation plan:	Yes