MHRA
10 South Colonnade
Canary Wharf
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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

MHRA-100711-PIP01-22-M01

Scope of the Application

Active Substance(s)

TISAGENLECLEUCEL

Condition(s)

Treatment of B cell acute lymphoblastic leukaemia/lymphoblastic lymphoma

Pharmaceutical Form(s)

Dispersion for infusion

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Novartis Pharmaceuticals UK Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Novartis Pharmaceuticals UK Limited submitted to the licensing authority on 29/09/2022 16:12 BST an application for a Modification

The procedure started on 01/03/2023 10:44 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

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-100711-PIP01-22-M01

Of 16/03/2023 10:05 GMT

On the adopted decision for TISAGENLECLEUCEL (MHRA-100711-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 Modification for TISAGENLECLEUCEL, Dispersion for infusion , INTRAVENOUS USE .

This decision is addressed to Novartis Pharmaceuticals UK Limited , Novartis Pharmaceuticals UK Limited 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, UNITED KINGDOM, W12 2FQ

ANNEX I

1. Waiver

1.1 Condition:

Treatment of B cell acute lymphoblastic leukaemia/lymphoblastic lymphoma The waiver applies / applied to: Paediatric Subset(s): The paediatric population weighing less than 6 kg Pharmaceutical form(s): Dispersion for 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 B cell acute lymphoblastic leukaemia/lymphoblastic lymphoma

2.2 Indication(s) targeted by the PIP:

Treatment of CD19+ B cell acute lymphoblastic leukaemia (ALL) in paediatric patients whose disease is refractory to a standard chemotherapy regimen, relapsed after stem cell transplantation (SCT) or are ineligible for allogenic SCT.

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

The paediatric population less than 18 years of age and weighing at least 6 kg

2.4 Pharmaceutical Form(s):

Dispersion for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	4	Study 1 (CHP959) Open-label, single-arm, posology-finding study to evaluate safety and feasibility of administration of redirected autologous T cells engineered to contain anti-CD19 attached to TCRzeta and 4-1BB signalling domains (CAR-19 cells) in patients from 1 year to less than 18 years of age (and adults) with a chemotherapy-resistant or refractory CD19+ leukaemia or lymphoma. Study 2 (14BT022/ CCTL019B2205J) Open-label, single-arm, single-dose study to evaluate safety and activity of tisagenlecleucel in patients from 3 to less than 18 years of age (and adults) with CD19+ B-cell acute lymphoblastic leukaemia/CD19+ B cell lymphoblastic lymphoma whose disease is refractory to a standard chemotherapy regimen, relapsed after stem cell transplantation (SCT) or are otherwise ineligible for allogeneic SCT. Study 3 (CCTL019B2202) Open-label, single-arm, single-

		dose study to evaluate safety and activity of tisagenlecleucel in patients from 3 to less than 18 years of age (and adults) with CD19+ B cell acute lymphoblastic leukaemia (ALL) whose disease is refractory to a standard chemotherapy regimen, relapsed after stem cell transplantation (SCT) or are otherwise ineligible for allogeneic SCT. Study 4 (CCTL019B210X) deleted in procedure EMEA-001654-PIP01-14-M03. Study 5 (CCTL019G2201J) (added in procedure EMEA-001654-PIP01-14-M03) Open-label, single-arm study to evaluate the efficacy and safety of tisagenlecleucel in de novo high-risk paediatric patients from 1 year to less than 18 years of age (and adults) with B-cell acute lymphoblastic leukaemia (B-ALL) who have positive minimal residual disease at the end of consolidation therapy.
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:	Yes
Date of completion of the paediatric investigation plan:	30/11/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes