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

MHRA-100160-PIP01-21-M01

Scope of the Application

Active Substance(s)

TOCILIZUMAB

Condition(s)

Cytokine release syndrome due to (CAR) T cell therapy or T-cell- bispecific antibody therapy

Pharmaceutical Form(s)

Concentrate for solution for infusion; solution for injection

Route(s) of Administration

Intravenous use; subcutaneous use

Name / Corporate name of the PIP applicant

Roche Products Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Roche Products Limited submitted to the licensing authority on 07/07/2021 18:07 BST an application for a Modification

The procedure started on 19/10/2021 15:33 BST

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-100160-PIP01-21-M01

Of 11/11/2021 07:12 GMT

On the adopted decision for TOCILIZUMAB (MHRA-100160-PIP01-21-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 TOCILIZUMAB, Concentrate for solution for infusion; solution for injection , Intravenous use .

This decision is addressed to Roche Products Limited, 6 Falcon Way, Shire Park, WELWYN GARDEN CITY, United Kingdom, AL7 1TW

ANNEX I

1. Waiver

1.1 Condition:

Treatment of cytokine release syndrome associated with chimeric antigen receptor (CAR) T cell therapy or T-cell- engaging bispecific antibody therapy The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Concentrate for solution for infusion; solution for injection Route(s) of administration: Intravenous use; subcutaneous 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 cytokine release syndrome associated with chimeric antigen receptor (CAR) T cell therapy or T-cell- engaging bispecific antibody therapy

2.2 Indication(s) targeted by the PIP:

Treatment of chimeric antigen receptor (CAR) T cell induced severe or life-threatening cytokine release syndrome (CRS) in paediatric patients 2 years of age and older Treatment of T-cell-engaging bispecific antibody-induced severe or life-threatening CRS in paediatric patients 2 years of age or older

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

All subsets of the paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Concentrate for solution 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	0	Not applicable
Extrapolation, Modeling & Simulation Studies	2	Study 2 Population PK model Modelling and simulation study to support the dosing recommendation of RoActemra (tocilizumab) in the treatment of T-cell-engaging bispecific antibody-induced CRS in children aged 2 to less than 18 years of age Study 3 Analysis of available data on the use of tocilizumab for the treatment of severe or life-threatening CRS induced by T-cell engaging bispecific antibodies in paediatric patients aged 2 years of age or older.
Other Studies	0	Not applicable
Other Measures	1	Study 1 Review of available data on use of tocilizumab in treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) (in adults and) paediatric patients 2 years of age and older

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:	31/12/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes