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-100028-PIP01-21-M01

Scope of the Application

Active Substance(s)

TIXAGEVIMAB; CILGAVIMAB

Condition(s)

Prevention of Coronavirus Disease 2019 (COVID-19), Treatment of COVID-19

Pharmaceutical Form(s)

Solution for injection/ infusion

Route(s) of Administration

Intramuscular use; Intravenous use

Name / Corporate name of the PIP applicant

AstraZeneca UK Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, AstraZeneca UK Ltd submitted to the licensing authority on 26/05/2022 09:49 BST an application for a Modification

The procedure started on 20/06/2022 11:00 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:

The acceptance of change 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-100028-PIP01-21-M01

Of 22/07/2022 13:36 BST

On the adopted decision for TIXAGEVIMAB; CILGAVIMAB (MHRA-100028-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 TIXAGEVIMAB; CILGAVIMAB, Solution for injection/ infusion , Intramuscular use, Intravenous use .

This decision is addressed to AstraZeneca UK Ltd, 2 Pancras Square, 8th Floor, London, UNITED KINGDOM, N1C 4AG

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Condition 1: Prevention of Coronavirus Disease 2019 (COVID-19); Condition 2: Treatment of Coronavirus Disease 2019 (COVID-19)

2.2 Indication(s) targeted by the PIP:

Condition 1: Pre-exposure prophylaxis of Coronavirus Disease 2019 (COVID-19) in children who are at risk of progressing to severe disease; Condition 2: Treatment of paediatric patients with

Coronavirus Disease 2019 (COVID-19) who are at risk of progressing to severe disease. Treatment of paediatric patients with severe coronavirus disease

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

For both conditions: All subsets of the paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

For both conditions: Solution for injection/ infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable
Non-Clinical Studies	0	Not applicable
Clinical Studies	1	Same study for both Prevention and Treatment of Coronavirus Disease 2019 (COVID-19) Study 1 (D8850C00006) Open label, uncontrolled, single dose study to evaluate pharmacokinetics (PK), pharmacodynamics (PD) and safety of tixagevimab and cilgavimab in paediatric subjects from 29 weeks gestational age (GA) to less than 18 years of age for: • Pre-exposure prophylaxis at high risk of developing severe COVID-19.(Cohort 1) • Treatment of paediatric patients with mild to moderate COVID-19 at high risk for developing severe disease (Cohort 2) • Treatment of severe COVID-19 (Cohort 3)
Extrapolation, Modeling & Simulation Studies	2	Same studies for both Prevention and Treatment of Coronavirus Disease 2019 (COVID-19) Study 2 A two-compartment population PK model (PopPK) for tixagevimab and cilgavimab dose prediction and confirmation in paediatric patients form 29 weeks gestational age (GA) to less than 18 years of age. Study 3 PK bridging and extrapolation of clinical efficacy and safety to the support use of tixagevimab and cilgavimab for: • Pre-exposure prophylaxis of COVID-19 (IV

		and IM routes) from adults at risk of developing severe disease, to children from 29 weeks gestational age to less than 18 years of age at risk of developing severe disease. • Treatment of mild-moderate COVID-19 (IV and IM routes) from adults with mild-moderate COVID-19 at risk of developing severe disease to children from 29 weeks gestational age to less than 18 years of age with mild-moderate COVID-19 at risk of developing severe disease. • Treatment of severe COVID-19 (IV route) from adults with severe COVID-19 to children from 29 weeks gestational age to less than 18 years of age with severe COVID-19. Study 4 Deleted during procedure MHRA-100028-PIP01-21-M01.
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:	30/06/2024
Deferral of one or more studies contained in the paediatric investigation plan:	Yes