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-100065-PIP01-21-M01

Scope of the Application

Active Substance(s)

TICAGRELOR

Condition(s)

Prevention of thromboembolic events

Pharmaceutical Form(s)

Tablet, Film-coated tablet, Orodispersible tablet

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

AstraZeneca UK Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, AstraZeneca UK Limited submitted to the licensing authority on 23/04/2021 17:54 BST an application for a Modification

The procedure started on 13/09/2021 18:42 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-100065-PIP01-21-M01

Of 20/09/2021 21:14 BST

On the adopted decision for TICAGRELOR (MHRA-100065-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 TICAGRELOR, Tablet, Film-coated tablet, Orodispersible tablet , Oral use .

This decision is addressed to AstraZeneca UK Limited, 600 Capability Green, Luton, United Kingdom, LU1 3LU

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Prevention of thromboembolic events

2.2 Indication(s) targeted by the PIP:

Prevention of vaso-occlusive crisis in paediatric patients with sickle cell disease

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

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

2.4 Pharmaceutical Form(s):

Film-coated tablet; Orodispersible tablet; Tablet

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Study 1 deleted in procedure EMEA-000480-PIP01-08-M11 Study 11 deleted in procedure MHRA-100065-PIP01-21-M01 Study 16 deleted in procedure MHRA-100065-PIP01-21-M01
Non-Clinical Studies	4	Study 2 Dose Range-Finding Study in Suckling Rats Study 3 Definitive study in Suckling Rats Study 4 Definitive Study in Weaning Rats Study 5 Suckling rat lung function study
Clinical Studies	4	Study 12 A two-part study with part A multi-centre, open-label, randomised, PK and PD dose-ranging study to determine dose and part B double-blind, parallel-group, placebo-controlled, 4-week extension in patients with sickle cell disease from 2 to less than 18 years of age. (D5136C00007) Study 13 Multi-centre, double-blind, randomised, placebo-controlled study to compare the effect of ticagrelor versus placebo for the reduction of vaso-occlusive crises (which is the composite of painful crisis and/or acute chest syndrome) in paediatric patients with sickle cell disease from 2 to less than 18 years of age. (D5136C00009) Study 14 Multi-centre, open label, single dose study to investigate the pharmacokinetics of ticagrelor in paediatric patients from birth to less than 24 months of age with

		sickle cell disease. (D5136C00010) Study 15 Open-label, randomised, 4-period, 4-treatment, crossover, single centre, single-dose study to assess the relative bioavailability of ticagrelor in different formulations in healthy adult subjects
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:	31/03/2021
Deferral of one or more studies contained in the paediatric investigation plan:	Yes