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-100040-PIP01-21-M01

Scope of the Application

Active Substance(s)

cotadutide

Condition(s)

Treatment of Type 2 Diabetes Mellitus

Pharmaceutical Form(s)

Solution for injection

Route(s) of Administration

Subcutaneous 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 15/02/2021 19:54 GMT an application for a Modification

The procedure started on 01/11/2021 11:16 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-100040-PIP01-21-M01

Of 10/11/2021 16:51 GMT

On the adopted decision for cotadutide (MHRA-100040-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 cotadutide, Solution for injection , Subcutaneous use .

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

ANNEX I

1. Waiver

1.1 Condition:

Treatment of Type 2 Diabetes Mellitus The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 10 years of age Pharmaceutical form(s): Solution for injection Route(s) of administration: Subcutaneous use Reason for granting waiver: on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of Type 2 Diabetes Mellitus

2.2 Indication(s) targeted by the PIP:

Treatment of Type 2 Diabetes Mellitus, as an adjunct to diet and exercise and metformin with or without additional insulin

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

The paediatric population from 10 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Solution for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable
Non-Clinical Studies	1	Study 1 Nonclinical pharmacokinetic / tissue distribution study in rats to investigate potential brain penetration of MEDI0382
Clinical Studies	2	Study 2 Open-label, uncontrolled multiple-dose study to explore the pharmacokinetics (PK) and pharmacodynamics (PD) of MEDI0382 and confirm a suitable dose for the subsequent pivotal paediatric study (Part A) Study 3 Randomised, double-blind, placebo-controlled, 26-week confirmatory study with a 26-week open label extension period to evaluate the efficacy and safety of MEDI0382 (Part B)
Extrapolation, Modeling & Simulation Studies	3	Study 4 Population PK/PD model to help characterize MEDI0382's dose-exposure-response after SC administration and to support dose selection in the paediatric PK/ PD clinical trial (Study 2, Part A) Study 5 Population PK/PD model to help characterize MEDI0382's dose-exposure-response after SC administration and to support dose selection in the confirmatory paediatric clinical trial (Study 3 Part B) Study 6 Population PK/PD model based on

		paediatric MEDI0382 PK and PD data from children aged 10 years to less than 18 years of age Study 2, Part A, and Study 3 Part B) 1. to characterise the paediatric PK using population PK modelling and identify the relevant PK covariates and 2. to explore the exposure-response in paediatrics and support paediatric dosing
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:	30/11/2024
Deferral of one or more studies contained in the paediatric investigation plan:	Yes