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-100039-PIP01-21-M01

Scope of the Application

Active Substance(s)

Cotadutide

Condition(s)

Treatment of non-alcoholic steatohepatitis (NASH)

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 19:10 GMT an application for a Modification

The procedure started on 01/11/2021 11:12 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-100039-PIP01-21-M01

Of 10/11/2021 13:48 GMT

On the adopted decision for Cotadutide (MHRA-100039-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 non-alcoholic steatohepatitis (NASH) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 8 years of age Pharmaceutical form(s): Solution for injection Route(s) of administration: Subcutaneous use Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments;

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of non-alcoholic steatohepatitis (NASH)

2.2 Indication(s) targeted by the PIP:

Treatment of non-cirrhotic NASH with fibrosis in children and adolescents

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

The paediatric population from 8 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 cotadutide.
Clinical Studies	2	Study 2 Double-blind, randomised placebo-controlled study, multiple dose pharmacokinetic/ pharmacodynamic (PK/PD) study to evaluate the PK and PD properties of cotadutide with slow up-titration in children and adolescents aged from 8 to less than 18 years with non-cirrhotic non-alcoholic steatohepatitis (Part A). Study 3 Confirmatory double-blind, randomised placebo-controlled study to evaluate the safety and efficacy of cotadutide in children and adolescents aged from 8 to less than 18 years with non-cirrhotic non-alcoholic steatohepatitis with fibrosis (Part B).
Extrapolation, Modeling & Simulation Studies	3	Study 4 Adult population pharmacokinetic (popPK) modelling and exposure-response relationship data will be used to simulate the effect of different dosing approaches on predicted paediatric exposure to inform dosing in the paediatric PK/PD study (study 2). Study 5 Paediatric PopPK modeling and exposure-response relationship data from

		adults will be used to simulate the effect of different dosing approaches on predicted paediatric exposure to inform dosing in the paediatric confirmatory study (study 3). Study 6 Paediatric PopPK model update with data from paediatric confirmatory study (Part B) to analyse the relationship between PK parameters and PD response of relevant clinical outcomes.
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:	31/12/2034
Deferral of one or more studies contained in the paediatric investigation plan:	Yes