

EMA/621041/2020

## European Medicines Agency decision

P/0452/2020

of 1 December 2020

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for cotadutide (EMEA-002712-PIP01-19) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

### **Disclaimer**

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

**Only the English text is authentic.**

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004<sup>1</sup>,

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency<sup>2</sup>,

Having regard to the application submitted by AstraZeneca AB on 16 December 2019 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 October 2020, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

- (1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.
- (2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.
- (3) It is therefore appropriate to adopt a decision granting a deferral.
- (4) It is therefore appropriate to adopt a decision granting a waiver.

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<sup>1</sup> OJ L 378, 27.12.2006, p.1.

<sup>2</sup> OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

**Article 1**

A paediatric investigation plan for cotadutide, solution for injection, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

**Article 2**

A deferral for cotadutide, solution for injection, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

**Article 3**

A waiver for cotadutide, solution for injection, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

**Article 4**

This decision is addressed to AstraZeneca AB, SE-151 85- Sodertalje, Sweden.

EMA/PDCO/401159/2020  
Amsterdam, 16 October 2020

## Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMA-002712-PIP01-19

### 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 AB

### Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, AstraZeneca AB submitted for agreement to the European Medicines Agency on 16 December 2019 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 28 January 2020.

Supplementary information was provided by the applicant on 1 July 2020. The applicant proposed modifications to the paediatric investigation plan.

## Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

- to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
- to grant a deferral in accordance with Article 21 of said Regulation;
- to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annex and appendix.

## **Annex I**

**The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)**

# 1. Waiver

Treatment of non-alcoholic steatohepatitis (NASH)

The waiver applies to:

- the paediatric population from birth to less than 8 years of age;
- solution for injection, subcutaneous use;
- 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:

Treatment of non-alcoholic steatohepatitis (NASH)

#### 2.1.1. Indication(s) targeted by the PIP

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

#### 2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 8 years to less than 18 years of age

#### 2.1.3. Pharmaceutical form(s)

Solution for injection

#### 2.1.4. Measures

| Area                    | Number of measures | Description                                                                                                                                                                                                                                                                                                                   |
|-------------------------|--------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Quality-related studies | 0                  | Not applicable.                                                                                                                                                                                                                                                                                                               |
| Non-clinical studies    | 1                  | <b>Study 1</b><br>Nonclinical pharmacokinetic/ tissue distribution study in rats to investigate potential brain penetration of cotadutide.                                                                                                                                                                                    |
| Clinical studies        | 2                  | <b>Study 2</b><br>Double-blind, randomised placebo-controlled, 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). |

|                                                 |   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-------------------------------------------------|---|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                 |   | <b>Study 3</b><br>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, modelling and simulation studies | 3 | <b>Study 4</b><br>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).<br><b>Study 5</b><br>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).<br><b>Study 6</b><br>Paediatric PopPK model update with data from paediatric confirmatory study (study 3) 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 PIP

|                                                                                       |                   |
|---------------------------------------------------------------------------------------|-------------------|
| Concerns on potential long-term safety/efficacy issues in relation to paediatric use: | Yes               |
| Date of completion of the paediatric investigation plan:                              | By December 2034. |
| Deferral for one or more measures contained in the paediatric investigation plan:     | Yes               |