EMA/366238/2022

European Medicines Agency decision

P/0217/2022

of 10 June 2022

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for cedazuridine / decitabine (EMEA-003071-PIP01-21) 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[1],

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

Having regard to the application submitted by Otsuka Pharmaceutical Netherlands B.V. on 12 July 2021 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 22 April 2022, in accordance with Article 17 of Regulation (EC) No 1901/2006 and of its own motion in accordance with 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.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for cedazuridine / decitabine, film-coated tablet, age appropriate oral solid dosage form, oral use, gastric 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 cedazuridine / decitabine, film-coated tablet, age appropriate oral solid dosage form, oral use, gastric 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 cedazuridine / decitabine, film-coated tablet, age appropriate oral solid dosage form, oral use, gastric 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 Otsuka Pharmaceutical Netherlands B.V., Herikerbergweg 292, 1101 CT – Amsterdam, The Netherlands.

EMA/78165/2022
Amsterdam, 22 April 2022

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

EMEA-003071-PIP01-21

Scope of the application

Active substance(s):

Cedazuridine / decitabine

Condition(s):

Treatment of acute myeloid leukaemia

Pharmaceutical form(s):

Film-coated tablet

Age appropriate oral solid dosage form

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

Otsuka Pharmaceutical Netherlands B.V.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Otsuka Pharmaceutical Netherlands B.V. submitted for agreement to the European Medicines Agency on 12 July 2021 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 17 August 2021.

Supplementary information was provided by the applicant on 24 January 2022. The applicant proposed modifications to the paediatric investigation plan and waiver.

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 of its own motion 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 Paediatric Committee member of Norway 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

1.1. Condition:

Treatment of acute myeloid leukaemia

The waiver applies to:

- the paediatric population from birth to less than 3 months of age;
- film-coated tablet, age appropriate oral solid dosage form, oral use, gastric use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of acute myeloid leukaemia (AML)

2.1.1. Indication(s) targeted by the PIP

To reduce measurable residual disease (MRD) in patients with high-risk de novo acute myeloid leukaemia (AML), therapy-related AML, or relapsed or refractory AML who have minimal residual disease (MRD) positivity after standard induction therapy and who will receive a myeloablative, allogeneic hematopoietic stem cell transplant (HSCT)

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

From 3 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet, age appropriate oral solid dosage form

2.1.4. Measures

Area	**Description**
Quality-related studies	**Study 1** Development of an age appropriate oral solid formulation
Non-clinical studies	Not applicable.
Clinical studies	**Study 2 (ASTX727-P01)** Open-label, multiple dose, trial to determine the recommended dose for Study 3 (ASTX727-P02), evaluate pharmacokinetics, pharmacodynamics, safety and activity of cedazuridine / decitabine in combination with venetoclax in children from 3 months to less than 18 years of age with relapsed/ refractory AML.

	Study 3 (ASTX727-P02) Open-label, randomised, controlled trial to evaluate safety, efficacy, acceptability/palatability of cedazuridine / decitabine in combination with venetoclax in children from 3 months to less than 18 years of age with AML who have minimal residual disease (MRD) positivity after standard induction therapy and who will receive a myeloablative, allogeneic hematopoietic stem cell transplant (HSCT) compared to HSCT alone.
Extrapolation, modelling and simulation studies	**Study 4** Modelling and simulation study to evaluate the use of cedazuridine / decitabine in combination with venetoclax in the proposed paediatric indication in children from 3 months to less than 18 years of age.
Other studies	Not applicable.
Other measures	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By December 2035
Deferral for one or more measures contained in the paediatric investigation plan:	Yes