



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/564095/2023

European Medicines Agency decision P/0543/2023

of 21 December 2023

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, (EMA-003071-PIP02-23) 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 726/2004¹,

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 Agency²,

Having regard to the application submitted by Otsuka Pharmaceutical Netherlands B.V. on 17 March 2023 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 15 December 2023, 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, following a re-examination procedure of the Paediatric Committee's opinion according to Article 25(3) of Regulation (EC) No 1901/2006, 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.



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/548049/2023
Amsterdam, 15 December 2023

Final opinion of the Paediatric Committee on the agreement of a Paediatric Investigation plan and a deferral and a waiver

EMA-003071-PIP02-23

Scope of the application

Active substance(s):

Cedazuridine / decitabine

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of myelodysplastic syndromes, including juvenile myelomonocytic 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 17 March 2023 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.



An Opinion was adopted by the Paediatric Committee on 10 November 2023 for the above mentioned product. Otsuka Pharmaceutical Netherlands B.V. received the Paediatric Committee Opinion on 20 November 2023.

On 30 November 2023 Otsuka Pharmaceutical Netherlands B.V. submitted to the European Medicines Agency a written request, including detailed grounds for re-examination of the Opinion.

The re-examination procedure started on 1 December 2023.

Final Opinion

1. The Paediatric Committee, having assessed the detailed grounds for re-examination, in accordance with Article 25(3) of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

1.1. to revise its opinion and

- 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.

1.2. following re-examination, to amend the measures and the timelines of the deferral.

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 annexes 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 myelodysplastic syndromes, including juvenile myelomonocytic 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 myelodysplastic syndromes, including juvenile myelomonocytic leukaemia

2.1.1. Indication(s) targeted by the PIP

Treatment of patients who require therapy to achieve remission prior to hematopoietic stem cell transplantation (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) (same as PIP study 2 for EMEA-003071-PIP01-21) Open-label, multiple dose, two part trial to determine the recommended dose for PIP Study 3 (ASTX727-P02), to 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

	acute myeloid leukaemia (AML), myelodysplastic neoplasms (MDS), including de novo MDS and juvenile myelomonocytic leukaemia (JMML).
Modelling and simulation studies	Study 3 (same as PIP study 4 for EMEA-003071-PIP01-21) 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.
Extrapolation plan	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 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.