EMADOC-1700519818-1789714

European Medicines Agency decision

EMA/PE/0000182217

of 6 December 2024

on the acceptance of a modification of an agreed paediatric investigation plan for cedazuridine / decitabine (Inaqovi) 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.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
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on the acceptance of a modification of an agreed paediatric investigation plan for cedazuridine / decitabine (Inaqovi) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 European Medicines Agency's decision P/0217/2022 issued on 10 June 2022 and the decision P/0124/2024 issued on 11 April 2024,

Having regard to the application submitted by Otsuka Pharmaceutical Netherlands B.V. on 28 June 2024 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 18 October 2024, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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 acceptance of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[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

Changes to the agreed paediatric investigation plan for cedazuridine / decitabine (Inaqovi), are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Otsuka Pharmaceutical Netherlands B.V. 292 Herikerbergweg, 1101 - CT Amsterdam Noord-Holland, The Netherlands.

EMADOC-1700519818-1616323
Amsterdam, 18 October 2024

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMA/PE/0000182217

Scope of the application

Active substance(s):

Cedazuridine /decitabine

Invented name and authorisation status:

See Annex II

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 22 of Regulation (EC) No 1901/2006 as amended, Otsuka Pharmaceutical Netherlands B.V. submitted to the European Medicines Agency on 28 June 2024 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0217/2022 issued on 10 June 2022 and the decision P/0124/2024 issued on 11 April 2024.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 19 August 2024.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

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

2. The measures and timelines of the 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 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, myelodysplastic

	neoplasms (MDS), including de novo MDS and juvenile myelomonocytic leukaemia (JMML). **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

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of AML

Authorised indication(s):

- Monotherapy for the treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) who are ineligible for standard induction chemotherapy.
  - Invented name(s): Inaqovi
  - Authorised pharmaceutical form(s): film-coated tablets
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure