

MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and grant a waiver

MHRA-100635-PIP02-24

Scope of the Application

Active Substance(s)

CEDAZURIDINE; DECITABINE

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 the Decision

Pursuant to the Human Medicines Regulations 2012, Otsuka Pharmaceutical Netherlands B.V. submitted to the licensing authority on 09/05/2024 14:32 BST an application for a Paediatric Investigation Plan

The procedure started on 04/06/2024 17:08 BST

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 agree a paediatric investigation plan and grant a deferral and grant a waiver

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-100635-PIP02-24

Of 09/09/2024 08:31 BST

On the adopted decision for CEDAZURIDINE; DECITABINE (MHRA-100635-PIP02-24) 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 a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for CEDAZURIDINE; DECITABINE, Film-coated tablet Age-appropriate oral solid dosage form , ORAL USE GASTRIC USE .

This decision is addressed to Otsuka Pharmaceutical Netherlands B.V., Herikerbergweg 292, Amsterdam, NETHERLANDS, 1101 CT

ANNEX I

1. Waiver

1.1 Condition:

Treatment of myelodysplastic syndromes, including juvenile myelomonocytic leukaemia The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 3 months of age Pharmaceutical form(s): Film-coated tablet Age-appropriate oral solid dosage form Route(s) of administration: ORAL USE GASTRIC USE Reason for granting waiver: 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(s):

Treatment of myelodysplastic syndromes, including juvenile myelomonocytic leukaemia

2.2 Indication(s) targeted by the PIP:

Treatment of patients who require therapy to achieve remission prior to hematopoietic stem cell transplantation (HSCT)

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

The paediatric population from 3 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

Film-coated tablet Age-appropriate oral solid dosage form

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	(Study 1 is the same as Study 1 for MHRA-100635-PIP01-22 and subsequent modifications thereof) Study 1 Development of an age-appropriate oral solid formulation.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	1	(Study 2 is the same as Study 2 for MHRA-100635-PIP01-22 and subsequent modifications thereof) Study 2 (ASTX727-P01) Open-label, multiple dose two part trial to determine the recommended dose for Study ASTX727-P02, evaluate the pharmacokinetics (PK), pharmacodynamics (PD), 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 (R/R) acute myeloid leukaemia (AML), myelodysplastic neoplasms (MDS), including de novo MDS and juvenile myelomonocytic leukaemia (JMML).
Extrapolation, Modeling & Simulation Studies	1	(Study 3 is the same as Study 4 for MHRA-100635-PIP01-22 and subsequent modifications thereof.) Study 3 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	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:	No
Date of completion of the paediatric investigation plan:	31/12/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes