MHRA
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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-PIP01-22

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 the Decision

Pursuant to the Human Medicines Regulations 2012, Otsuka Pharmaceutical Netherlands B.V. submitted to the licensing authority on 29/07/2022 16:03 BST an application for a Paediatric Investigation Plan

The procedure started on 23/01/2023 08:24 GMT

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-PIP01-22

Of 20/02/2023 07:47 GMT

On the adopted decision for CEDAZURIDINE ; DECITABINE (MHRA-100635-PIP01-22) 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 acute myeloid 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 acute myeloid leukaemia (AML)

2.2 Indication(s) targeted by the PIP:

To reduce measurable residual disease (MRD) in patients with high-risk de novo AML, therapy-related AML, or relapsed or refractory AML who have MRD positivity after standard induction therapy and who will receive a myeloablative, allogeneic hematopoietic stem cell transplant (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 Development of an age-appropriate oral solid formulation.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	2	Study 2 (ASTX727-P01) Open-label, multiple dose trial to determine the recommended dose for Study 3 (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). 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 haematopoietic stem cell transplant (HSCT), compared to HSCT alone.

Extrapolation, Modeling & Simulation Studies	1	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	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:	31/12/2035
Deferral of one or more studies contained in the paediatric investigation plan:	Yes