MHRA
10 South Colonnade
Canary Wharf
London
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United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral.

MHRA-100352-PIP01-21-M03

Scope of the Application

Active Substance(s)

AVAPRITINIB

Condition(s)

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms)

Pharmaceutical Form(s)

Film-coated tablet; Age-appropriate oral solid dosage form

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Blueprint Medicines (Netherlands) B.V.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Blueprint Medicines (Netherlands) B.V. submitted to the licensing authority on 30/08/2024 11:22 BST an application for a Modification

The procedure started on 18/09/2024 13:08 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 accept change(s) to the agreed paediatric investigation plan and to the deferral.

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-100352-PIP01-21-M03

Of 05/11/2024 10:33 GMT

On the adopted decision for AVAPRITINIB (MHRA-100352-PIP01-21-M03) 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 modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan).

This decision applies to a Modification for AVAPRITINIB, Film-coated tablet; Age-appropriate oral solid dosage form , ORAL USE .

This decision is addressed to Blueprint Medicines (Netherlands) B.V., Gustav Mahlerplein 2, Amsterdam, NETHERLANDS, 1082 MA

ANNEX I

1. Waiver

1.1 Condition:

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age. Pharmaceutical form(s): Film-coated tablet; Age-appropriate oral solid dosage form Route(s) of administration: ORAL USE Reason for granting waiver: On the grounds the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms).

2.2 Indication(s) targeted by the PIP:

Treatment of paediatric patients from 2 years to less than 18 years of age with a relapsed/ refractory solid tumour harbouring mutations in either KIT or PDGFR-alpha, KIT or PDGFR-alpha amplifications, or a diffuse-midline glioma with H3K27 alterations (DMG-H3K27a).

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

The paediatric population from 2 years 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 form.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	2	Study 2 (BLU-285-3101) Multicentre, open-label, single arm study to evaluate safety, pharmacokinetics (part 1) and anti-tumour activity (part 2) of avapritinib in paediatric patients from 2 years to less than 18 years of age with a relapsed/refractory solid tumour harbouring a mutation in KIT or PDGFR-alpha, KIT or PDGFR-alpha amplifications that has progressed despite standard therapy and for which there are no available alternative treatment options, or a diffuse-midline glioma with H3K27 alterations (DMG-H3K27a) that has failed standard therapy or for which no standard therapy may convey clinical benefits exists, as judged by the investigator. Study 3 (BLU-285-3303) Multicentre, open-label, randomised study to evaluate safety, pharmacokinetics and efficacy of avapritinib compared

		to investigator's choice of therapy in paediatric patients from 2 years to less than 18 years of age with a relapsed/refractory solid tumour harbouring a mutation in KIT or PDGFR-alpha, KIT or PDGFR-alpha amplifications, or a diffuse-midline glioma with H3K27 alterations (DMG-H3K27a) selected based on the results of Study 2.
Extrapolation, Modeling & Simulation Studies	1	Study 4 (AVA-PIP-M&S-1) Modelling and simulation study to evaluate the use and support dosing regimen of avapritinib in children and adolescents from 2 years to less than 18 years of age with a relapsed/ refractory solid tumour KIT or PDGFR-alpha.
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:	Yes
Date of completion of the paediatric investigation plan:	31/07/2030
Deferral of one or more studies contained in the paediatric investigation plan:	Yes