EMA/315615/2023

European Medicines Agency decision

P/0281/2023

of 14 July 2023

on the acceptance of a modification of an agreed paediatric investigation plan for avapritinib (Ayvakyt), (EMEA-002358-PIP02-18-M03) 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 726/2004[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/0026/2019 issued on 22 February 2019, the decision P/0007/2020 issued on 6 January 2020, and the decision P/0016/2022 issued on 31 January 2022,

Having regard to the application submitted by Blueprint Medicines (Netherlands) B.V. on 17 March 2023 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 23 June 2023, 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 avapritinib (Ayvakyt), film-coated tablet, age-appropriate oral solid dosage form, oral use, 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 Blueprint Medicines (Netherlands) B.V. Gustav Mahlerplein 2, 1082 MA - Amsterdam, The Netherlands.

EMA/PDCO/139803/2023
Amsterdam, 23 June 2023

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

EMEA-002358-PIP02-18-M03

Scope of the application

Active substance(s):

Avapritinib

Invented name and authorisation status:

See Annex II

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 opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Blueprint Medicines (Netherlands) B.V. submitted to the European Medicines Agency on 17 March 2023 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/0026/2019 issued on 22 February 2019, the decision P/0007/2020 issued on 6 January 2020, and the decision P/0016/2022 issued on 31 January 2022.

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

The procedure started on 24 April 2023.

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

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- film-coated tablet, age-appropriate oral solid dosage form, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition:

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

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from 2 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 H3K27M mutant glioma

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 2 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 form
Non-clinical studies	Not applicable
Clinical studies	**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 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 H3K27M mutant glioma and no available alternative treatment options. **Study 3** (BLU-285-3303) Multicentre, open-label, randomized study to evaluate safety, pharmacokinetics and efficacy of avapritinib compared to investigator's choice of therapy in paediatric patients from 2 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 H3K27M mutant glioma selected based on the results of Study 2.
Extrapolation, modelling and simulation studies	**Study 4** Modelling and simulation study to evaluate the use and support dosing regimen of avapritinib in children and adolescents from 2 to less than 18 years of age with a relapsed / refractory solid tumour KIT or PDGFR-alpha. (AVA-PIP-M&S-1)
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:	Yes
Date of completion of the paediatric investigation plan:	By July 2030
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 all conditions included in the category of malignant neoplasms (except haematopoietic and lymphoid tissue neoplasms)

Authorised indication(s):

- Ayvakyt is indicated as monotherapy for the treatment of adult patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) harbouring the platelet-derived growth factor receptor alpha (PDGFRA) D842V mutation.
  - Invented name(s): Ayvakyt
  - Authorised pharmaceutical form(s): Film-coated tablet
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure
  -

2. Treatment of mastocytosis

Authorised indication(s):

- Ayvakyt is indicated as monotherapy for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL), after at least one systemic therapy.
  - Invented name(s): Ayvakyt
  - Authorised pharmaceutical form(s): Film-coated tablet
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure