EMA/250923/2023

European Medicines Agency decision

P/0267/2023

of 14 July 2023

on the acceptance of a modification of an agreed paediatric investigation plan for gilteritinib (as fumarate), (Xospata), (EMEA-002064-PIP01-16-M05) 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/0006/2018 issued on 19 January 2018, decision P/0194/2019 issued on 15 May 2019, the decision P/0173/2020 issued on 13 May 2020, the decision P/0110/2021 issued on 17 March 2021 and the decision P/0069/2023 issued on 10 March 2023,

Having regard to the application submitted by Astellas Pharma Europe B.V. on 20 February 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 26 May 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.

Article 1

Changes to the agreed paediatric investigation plan for gilteritinib (as fumarate), (Xospata), film-coated tablet, age-appropriate oral 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 Astellas Pharma Europe B.V., Sylviusweg 62, 2333 BE - Leiden, The Netherlands.

EMA/PDCO/102837/2023 Corr[1]
Amsterdam, 26 May 2023

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

EMEA-002064-PIP01-16-M05

Scope of the application

Active substance(s):

Gilteritinib (as fumarate)

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of acute myeloid leukaemia

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Astellas Pharma Europe B.V.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Astellas Pharma Europe B.V. submitted to the European Medicines Agency on 20 February 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/0006/2018 issued on 19 January 2018, decision P/0194/2019 issued on 15 May 2019, the decision P/0173/2020 issued on 13 May 2020, the decision P/0110/2021 issued on 17 March 2021 and the decision P/0069/2023 issued on 10 March 2023.

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

[1] 01 June 2023

The procedure started on 27 March 2023.

Scope of the modification

Some measures 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 6 months of age;
- film-coated tablet, oral use, age-appropriate oral dosage form, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition

Treatment of acute myeloid leukaemia

2.1.1. Indication(s) targeted by the PIP

Treatment of patients from 6 months to less than 18 years of age with relapsed or refractory FLT3/ITD positive acute myeloid leukaemia or newly-diagnosed FLT3/ITD positive acute myeloid leukaemia

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

From 6 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate oral dosage form

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of film-coated tablets smaller and of lower strength (compared to the existing pharmaceutical form) and suitable to be administered as oral suspension and appropriate to children unable to swallow the adult-sized film-coated tablets

Non-clinical studies	**Study 2** Definitive juvenile rat study aimed to assess the toxicity of gilteritinib
Clinical studies	**Study 3** Open-label, single arm study to evaluate the pharmacokinetic, safety and anti-tumour activity of gilteritinib used in sequential combination with chemotherapy in paediatric patients from 6 months to less than 18 years of age (and young adults) with FLT3/ITD positive relapse/refractory acute myeloid leukaemia with a dose-finding phase (phase 1) and an expansion phase (phase 2) (2215-CL-0603) **Study 4** Open-label, single arm study to evaluate the pharmacokinetic, safety and efficacy of gilteritinib used in sequential combination with chemotherapy in paediatric patients from 6 months to less than 18 years of age (and young adults) with FLT3/ITD positive newly-diagnosed acute myeloid leukaemia (2215-CL-0604-gilteritinib in combination with standard chemotherapy arm)
Extrapolation, modelling and simulation studies	**Study 5** Modelling and simulation study to simulate and predict gilteritinib exposure in children from 6 months to less than 18 years of age with acute myeloid leukaemia **Study 6 (introduced during EMEA-002064-PIP01-16-M03)** Physiologically-based modelling study to simulate gilteritinib exposure in populations of children from 6 months to less than 18 years of age with AML
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 September 2026
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:

1. Treatment of acute myeloid leukaemia

Authorised indication(s):

- Xospata is indicated as monotherapy for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with a FLT3 mutation
  - Invented name(s): Xospata
  - Authorised pharmaceutical form(s): Film-coated tablets
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure