EMA/320725/2024

European Medicines Agency decision

P/0305/2024

of 16 August 2024

on the acceptance of a modification of an agreed paediatric investigation plan for midostaurin (Rydapt), (EMEA-000780-PIP01-09-M08) 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/6/2011 issued on 3 January 2011, the decision P/0296/2014 issued on 7 November 2014, the decision P/0039/2016 issued on 19 February 2016, the decision P/0011/2017 issued on 31 January 2017, the decision P/0027/2018 issued on 5 March 2018, the decision P/0086/2021 issued on 19 March 2021 and the decision P/0068/2024 issued on 8 March 2024,

Having regard to the application submitted by Novartis Europharm Limited on 21 March 2024 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 28 June 2024, 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 midostaurin (Rydapt), oral solution, capsule, soft, 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 Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, 4 – Dublin, Ireland.

EMA/PDCO/141563/2024
Amsterdam, 28 June 2024

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

EMEA-000780-PIP01-09-M08

Scope of the application

Active substance(s):

Midostaurin

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of acute myeloid leukaemia

Treatment of malignant mastocytosis

Treatment of mast cell leukaemia

Pharmaceutical form(s):

Oral solution

Capsule, soft

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Novartis Europharm Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted to the European Medicines Agency on 21 March 2024 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/6/2011 issued on 3 January 2011, the decision P/0296/2014 issued on 7 November 2014, the decision P/0039/2016 issued on 19 February 2016, the decision P/0011/2017

issued on 31 January 2017, the decision P/0027/2018 issued on 5 March 2018, the decision P/0086/2021 issued on 19 March 2021 and the decision P/0068/2024 issued on 8 March 2024.

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

The procedure started on 29 April 2024.

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:

- paediatric population from birth to less than 3 months of age;
- oral solution, capsule, soft, oral use;
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

1.2. Condition:

Treatment of malignant mastocytosis and treatment of mast cell leukaemia

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- oral solution, capsule, soft, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of acute myeloid leukaemia

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with FLT3 mutated AML, newly diagnosed.

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

From 3 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Oral solution

Capsule, soft

2.1.4. Measures

Area	Description
Quality-related measures	Not applicable.
Non-clinical studies	**Study 1** Juvenile development study.
Clinical studies	**Study 2** Open-label, dose-escalating, single-agent, multi-centre, age-stratified trial to evaluate toxicity, pharmacokinetics, pharmacodynamics, safety and activity of midostaurin in children from 3 months to less than 18 years of age with refractory or relapse acute lymphoblastic or acute myeloid leukaemia. **Study 3** Open-label, dose-escalating, multi-centre trial to evaluate toxicity, pharmacokinetics, pharmacodynamics, safety and activity in children from 3 months to less than 18 years of age with newly-diagnosed acute myeloid leukaemia with FLT3 mutations. **Study 4** Population pharmacokinetic / pharmacodynamic and outcome model to support extrapolation of efficacy.

3. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By December 2026
Deferral for one or more studies 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 acute myeloid leukaemia

Authorised indication(s):

- Rydapt is indicated: in combination with standard daunorubicin and cytarabine induction and high-dose cytarabine consolidation chemotherapy, and for patients in complete response followed by Rydapt single agent maintenance therapy, for adult patients with newly diagnosed acute myeloid leukaemia (AML) who are FLT3 mutation-positive
  - Invented name(s): Rydapt
  - Authorised pharmaceutical form(s): Capsules, soft
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure

2. Treatment of malignant mastocytosis

3. Treatment of mast cell leukaemia

- Rydapt is indicated as monotherapy for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN), or mast cell leukaemia (MCL).
  - Invented name(s): Rydapt
  - Authorised pharmaceutical form(s): Capsules, soft
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure