

EMA/20904/2017

## European Medicines Agency decision

P/0011/2017

of 31 January 2017

on the acceptance of a modification of an agreed paediatric investigation plan for midostaurin (EMEA-000780-PIP01-09-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.**

# European Medicines Agency decision

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on the acceptance of a modification of an agreed paediatric investigation plan for midostaurin (EMA-000780-PIP01-09-M03) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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<sup>1</sup>,

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency<sup>2</sup>,

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 and the decision P/0039/2016 issued on 19 February 2016,

Having regard to the application submitted by Novartis Europharm Ltd on 23 September 2016 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 16 December 2016, in accordance with Article 22 of Regulation (EC) No 1901/2006 and Article 20(1) of said 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 the changes to the agreed paediatric investigation plan and refusal of the changes to the deferral.
- (2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, and refusal of the changes to the deferral.

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<sup>1</sup> OJ L 378, 27.12.2006, p.1.

<sup>2</sup> OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

**Article 1**

Changes to the agreed paediatric investigation plan for midostaurin, 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**

Changes to the deferral for midostaurin, oral solution, capsule, soft, oral use, are hereby refused in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

**Article 3**

This decision is addressed to Novartis Europharm Ltd, Frimley Business Park, GU16 7SR - Camberley, United Kingdom.

EMA/PDCO/656018/2016  
London, 16 December 2016

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

EMA-000780-PIP01-09-M03

### Scope of the application

**Active substance(s):**

Midostaurin

**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 Ltd

### Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Ltd submitted to the European Medicines Agency on 23 September 2016 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 and P/0039/2016 issued on 19 February 2016.

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

The procedure started on 18 October 2016.

## **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
  - to refuse a change of deferral as it does not meet the grounds detailed in Article 20(1) of said Regulation.

The Norwegian Paediatric Committee member 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 annex 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;
- for oral solution and soft capsule for 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;
- for oral solution and soft capsule for 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                     | Number of measures | Description                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|--------------------------|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Quality-related measures | 0                  | Not applicable.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Non-clinical studies     | 1                  | <b>Study 1</b><br>Juvenile development study                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Clinical studies         | 3                  | <b>Study 2</b><br>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<br><b>Study 3</b><br>Open-label, dose-escalating, randomised, active-controlled, age-stratified, 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<br><b>Study 4</b><br>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 2019 |
| Deferral for one or more studies contained in the paediatric investigation plan:                  | Yes              |