EMA/537846/2018

European Medicines Agency decision

P/0293/2018

of 12 September 2018

on the acceptance of a modification of an agreed paediatric investigation plan for ponatinib (Iclusig), (EMEA-001186-PIP01-11-M02) 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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An agency of the European Union

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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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0131/2012 issued on 4 July 2012 and P/0127/2017 issued on 5 May 2017,

Having regard to the application submitted by Incyte Biosciences Distribution B.V on 7 May 2018 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 27 July 2018, 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 and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for ponatinib (Iclusig), film-coated tablet, capsule, hard, age-appropriate formulation, oral use, including changes to the deferral, 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 Incyte Biosciences Distribution B.V, Paasheuvelweg 25, 1105 BP– Amsterdam, The Netherlands.

EMA/PDCO/301144/2018 Corr
London, 27 July 2018

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

EMEA-001186-PIP01-11-M02

Scope of the application

Active substance(s):

Ponatinib

Invented name:

Iclusig

Condition(s):

Treatment of chronic myeloid leukaemia

Treatment of acute lymphoblastic leukaemia

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Capsule, hard

Age-appropriate formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Incyte Biosciences Distribution B.V

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Incyte Biosciences Distribution B.V submitted to the European Medicines Agency on 7 May 2018 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/0131/2012 issued on 4 July 2012 and P/0127/2017 issued on 5 May 2017.

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

The procedure started on 29 May 2018.

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 and to the deferral in the scope set out in the Annex I of this opinion.

   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 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 chronic myeloid leukaemia

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- film-coated tablet, capsule, hard, and age-appropriate formulation, 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).

1.2. Condition

Treatment of acute lymphoblastic leukaemia

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- film-coated tablet and capsule, hard, and age-appropriate formulation, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as the needs are already covered.

2. Paediatric Investigation Plan

2.1. Condition

Treatment of chronic myeloid leukaemia

2.1.1. Indication(s) targeted by the PIP

For the treatment of the paediatric population with chronic (CP), accelerated (AP), or blast phase (BP) CML who are resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy, or who have the T315I mutation

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

From 1 year to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Capsule, hard

Age-appropriate formulation

2.1.4. Measures

Area	Number of measures	
Quality	2	**Study 1** Development of an age-appropriate formulation for oral use. **Study 5** (added in procedure EMEA-001186-PIP01-11-M02) Development of capsules of 5 mg strength.
Non-clinical	1	**Study 2** Toxicity study in juvenile rats.
Clinical	1	**Study 3** Open-label, single-agent, dose-escalation, multi-centre trial to investigate tolerability, safety and activity of ponatinib in the paediatric population from 1 year to less than 18 years of age with malignant disease for which no effective treatment is known, and with an expansion cohort of the paediatric population with chronic phase chronic myeloid leukaemia.

2.2. Condition

Treatment of acute lymphoblastic leukaemia

2.2.1. Indication(s) targeted by the PIP

For the treatment of the paediatric population with Ph+ ALL who are resistant or intolerant to prior TKI therapy, or who have the T315I mutation

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

From 1 year to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Film-coated tablet

Capsule, hard

Age-appropriate formulation

2.2.4. Measures

Area	Number of measures	
Quality	2	**Study 1** As for condition "Treatment of chronic myeloid leukaemia".

		Study 5 (added in procedure EMEA-001186-PIP01-11-M02) As for condition "Treatment of chronic myeloid leukaemia".
Non-clinical	1	**Study 2** As for condition "Treatment of chronic myeloid leukaemia".
Clinical	2	**Study 3** As for condition "Treatment of chronic myeloid leukaemia". **Study 4** Open-label, multi-centre trial including a safety lead-in phase to investigate the safety, the activity and the efficacy of ponatinib as add-on to standard therapy in the paediatric population from 1 year to less than 18 years of age with relapsed or refractory BCR-ABL translocation-positive ALL.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By September 2024
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of chronic myeloid leukaemia

Authorised indication(s):

- Iclusig is indicated in adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukaemia (CML) who are resistant to dasatinib or nilotinib; who are intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation

2. Treatment of acute lymphoblastic leukaemia

Authorised indication(s):

- Iclusig is indicated in adult patients with Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) who are resistant to dasatinib; who are intolerant to dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use