EMA/871222/2018

European Medicines Agency decision

P/0021/2019

of 3 January 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for ibrutinib (Imbruvica), (EMEA-001397-PIP04-17) 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 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 application submitted by Janssen-Cilag International NV on 7 July 2017 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 November 2018, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

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

Has adopted this decision:

Article 1

A paediatric investigation plan for ibrutinib (Imbruvica), capsule, hard, film-coated tablet, oral suspension, oral use, gastric use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for ibrutinib (Imbruvica), capsule, hard, film-coated tablet, oral suspension, oral use, gastric use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for ibrutinib (Imbruvica), capsule, hard, film-coated tablet, oral suspension, oral use, gastric use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0252/2015 issued on 30/10/2015 including subsequent modifications thereof.

Article 5

This decision is addressed to Janssen-Cilag International N.V. Turnhoutseweg 30 B-2340 – Beerse, Belgium.

EMA/PDCO/575863/2018
London, 16 November 2018

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-001397-PIP04-17

Scope of the application

Active substance(s):

Ibrutinib

Invented name:

Imbruvica

Condition(s):

Treatment of chronic graft versus host disease (cGvHD)

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Capsule, hard

Film-coated tablet

Oral suspension

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

Janssen-Cilag International NV

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Janssen-Cilag International NV submitted for agreement to the European Medicines Agency on 7 July 2017 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 15 August 2017.

Supplementary information was provided by the applicant on 10 August 2018.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 graft versus host disease (cGvHD)

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- capsule, hard, film-coated tablet, oral suspension, oral use; gastric 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 chronic graft versus host disease (cGvHD)

2.1.1. Indication(s) targeted by the PIP

Treatment of chronic graft versus host disease (cGvHD)

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

From 1 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Capsule, hard

Film-coated tablet

Oral suspension

2.1.4. Measures

Area	**Number of measures**	**Description**
Quality-related studies	1	**Study 1: CMCPED01** Development of age-appropriate oral suspension and capsule, hard *This study is the same as study 1 of the ibrutinib PIP EMEA-001397-PIP03-14 and subsequent modifications thereof*
Non-clinical studies	0	Not applicable.

Clinical studies	2	**Study 2: PCYC-1140-IM** Randomized, double-blind study to evaluate efficacy, safety and tolerability of oral ibrutinib *versus* placebo on background regimen of corticosteroids in paediatric patients from 12 to less than 18 years of age (and adults) with new onset cGvHD **Study 3: PCYC-1146-IM** Open label uncontrolled study to evaluate dose-finding, pharmacokinetics, safety and activity of oral ibrutinib in paediatric patients from 1 to less than 18 years of age (and adults) with moderate or severe cGVHD.
Extrapolation, modelling and simulation studies	2	**Study 4** Population PK and PK/PD modelling and simulation study to support the use of ibrutinib in paediatric patients from 1 to less than 18 years of age with cGvHD **Study 5** Extrapolation study to support the use of ibrutinib in paediatric patients from 1 to less than 18 years of age with cGvHD
Other studies	0	Not applicable.
Other measures	0	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 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of mantle cell lymphoma

Authorised indication(s):

- IMBRUVICA as a single agent is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL)

2. Treatment of chronic lymphocytic leukaemia

Authorised indication(s):

- IMBRUVICA as a single agent is indicated for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL)
- IMBRUVICA as a single agent or in combination with bendamustine and rituximab (BR) is indicated for the treatment of adult patients with CLL who have received at least one prior therapy.

3. Treatment of lymphoplasmacytic lymphoma

Authorised indication(s):

- IMBRUVICA as a single agent is indicated for the treatment of adult patients with Waldenström's macroglobulinaemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy.

Authorised pharmaceutical form(s):

Capsule, hard

Authorised route(s) of administration:

Oral use