EMA/336523/2023

European Medicines Agency decision

P/0295/2023

of 11 August 2023

on the acceptance of a modification of an agreed paediatric investigation plan for ibrutinib (Imbruvica), (EMEA-001397-PIP04-17-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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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/0021/2019 issued on 3 January and the decision P/0421/2019 issued on 6 December 2019,

Having regard to the application submitted by Janssen-Cilag International NV on 14 March 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 23 June 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 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, 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 Ibrutinib (Imbruvica), capsule, hard, film-coated tablet, oral suspension, oral use, gastric 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 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 October 2015 including subsequent modifications thereof.

Article 3

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

EMA/PDCO/139642/2023
Amsterdam, 23 June 2023

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

EMEA-001397-PIP04-17-M02

Scope of the application

Active substance(s):

Ibrutinib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of chronic graft versus host disease

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

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Janssen-Cilag International NV submitted to the European Medicines Agency on 14 March 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/0021/2019 issued on 3 January and the decision P/0421/2019 issued on 6 December 2019.

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

The procedure started on 24 April 2023.

Scope of the modification

Some 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 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 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	Description
Quality-related studies	**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	Not applicable.
Clinical studies	**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	**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	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 January 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:

Condition(s) and authorised indication(s)

1. Treatment of mantle cell lymphoma

Authorised indication(s):

- as single agent indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL)
  - Invented name(s): Imbruvica
  - Authorised pharmaceutical form(s): Capsule, hard
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure

2. Treatment of chronic lymphocytic leukaemia

Authorised indication(s):

- as a single agent is indicated for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL)
- 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 therap
  - Invented name(s): Imbruvica
  - Authorised pharmaceutical form(s): Capsule, hard
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure

3. Treatment of lymphoplasmacytic lymphoma

Authorised indication(s):

- 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
  - Invented name(s): Imbruvica
  - Authorised pharmaceutical form(s): Capsule, hard
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure