EMA/93299/2021

European Medicines Agency decision

P/0117/2021

of 17 March 2021

on the acceptance of a modification of an agreed paediatric investigation plan for ibrutinib (Imbruvica), (EMEA-001397-PIP03-14-M05) 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 European Medicines Agency's decision P/0252/2015 issued on 30 October 2015, the decision P/0150/2016 issued on 14 June 2016, the decision P/0100/2017 issued on 11 April 2017, the decision P/0398/2017 issued on 19 December 2017 and the decision P/0201/2019 issued on 12 June 2019,

Having regard to the application submitted by Janssen-Cilag International N.V. on 26 October 2020 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 29 January 2021, 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 ibrutinib (Imbruvica), capsule, hard, film-coated tablet, 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 Janssen-Cilag International N.V., Turnhoutseweg 30, B-2340 – Beerse, Belgium.

EMA/PDCO/588177/2020
Amsterdam, 29 January 2021

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

EMEA-001397-PIP03-14-M05

Scope of the application

Active substance(s):

Ibrutinib

Invented name:

Imbruvica

Condition(s):

Treatment of mature B-cell neoplasm

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Capsule, hard

Film-coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Janssen-Cilag International N.V.

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Janssen-Cilag International N.V. submitted to the European Medicines Agency on 26 October 2020 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/0252/2015 issued on 30 October 2015, the decision P/0150/2016 issued on 14 June 2016, the decision P/0100/2017 issued on 11 April 2017, the decision P/0398/2017 issued on 19 December 2017 and the decision P/0201/2019 issued on 12 June 2019.

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

The procedure started on 1 December 2020.

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 mature B-cell neoplasm

The waiver applies to:

- the paediatric population from birth to less than 1 years of age;
- capsule, hard and film-coated tablet, 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 mature B-cell neoplasm

2.1.1. Indication(s) targeted by the PIP

Treatment of children from 1 year to less than 18 years of age with newly-diagnosed and relapsed/ refractory mature B-cell lymphoma, that is, diffuse large B-cell lymphoma or Burkitt and Burkitt-like lymphoma

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)

Capsule, hard

Film-coated tablet

2.1.4. Measures

Area	**Number of measures**	**Description**
Quality-related studies	0	**Study 1** *Deleted in procedure EMEA-001397- PIP03-14-M05.*
Non-clinical studies	1	**Study 2** In vitro and in vivo non-clinical efficacy studies of ibrutinib, including in combination, in models of paediatric malignant diseases

Clinical studies	1	**Study 3** Multi-centre, randomised add-on study with run-in phase to evaluate pharmacokinetics, pharmacodynamics, toxicity, safety and anti-tumour activity of ibrutinib as add-on to RICE or RVICI regimens in paediatric patients from 1 year to less than 18 years (and young adults) with a relapsed or refractory mature B cell lymphoma **Study 4** *Deleted in procedure EMEA-001397- PIP03-14-M05.*
Extrapolation, modelling and simulation studies	1	**Study 5** Physiologically-based pharmacokinetic (PBPK) model
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 December 2021
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 or in combination with rituximab or obinutuzumab 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. IMBRUVICA in combination with rituximab is indicated for the treatment of adult patients with WM.

Authorised pharmaceutical form(s):

Capsule, hard

Film-coated tablet

Authorised route(s) of administration:

Oral use