EMA/607434/2019

European Medicines Agency decision

P/0398/2019

of 4 December 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for zanubrutinib (EMEA-002354-PIP02-18) 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 BeiGene Ireland Ltd on 28 October 2018 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 18 October 2019, 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 zanubrutinib, capsule, hard, age-appropriate dosage form, oral use, naso-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 zanubrutinib, capsule, hard, age-appropriate dosage form, oral use, naso-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 zanubrutinib, capsule, hard, age-appropriate dosage form, oral use, naso-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 is addressed to BeiGene Ireland, Ltd, 10 Earlsfort Terrace, D02 T380 – Dublin, Ireland.

EMA/PDCO/414193/2019
Amsterdam, 18 October 2019

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

EMEA-002354-PIP02-18

Scope of the application

Active substance(s):

Zanubrutinib

Condition(s):

Treatment of lymphoplasmacytic lymphoma

Treatment of mature B-cell neoplasms (excluding lymphoplasmacytic lymphoma)

Pharmaceutical form(s):

Capsule, hard

Age-appropriate dosage form

Route(s) of administration:

Oral use

Naso-gastric use

Name/corporate name of the PIP applicant:

BeiGene Ireland Ltd

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, BeiGene Ireland Ltd submitted for agreement to the European Medicines Agency on 28 October 2018 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 4 December 2018.

Supplementary information was provided by the applicant on 15 July 2019. The applicant proposed modifications to the paediatric investigation plan.

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)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population.

   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 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 lymphoplasmacytic lymphoma

The waiver applies to:

- the paediatric population from birth to less than 18 years of age;
- capsule, hard, age-appropriate dosage form, oral use, naso-gastric 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 mature B-cell neoplasms (excluding lymphoplasmacytic lymphoma)

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- capsule, hard, age-appropriate dosage form, oral use, naso-gastric 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 neoplasms (excluding lymphoplasmacytic lymphoma)

2.1.1. Indication(s) targeted by the PIP

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

Age-appropriate dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Age-appropriate dosage form (e.g. mini-tablets, dispersible tablets, granules, pellets or oral suspension not containing commercial vehicles such as ORA-Plus or ORA-Sweet)
Non-clinical studies	1	**Study 2** *In vitro* and *in vivo* efficacy studies of zanubrutinib used in monotherapy and in combination with relevant chemotherapy, in models of paediatric B-cell malignancies.
Clinical studies	1	**Study 3** Open-label, single arm dose-escalation (phase 1) trial to evaluate the pharmacokinetics, pharmacodynamics, safety and anti-tumour activity of zanubrutinib as add-on to investigator's choice chemo-immunotherapy in paediatric patients from 1 to less than 18 years of age (and adults) with a relapsed or refractory mature B-cell neoplasm and an expansion cohort (phase 2).
Extrapolation, modelling and simulation studies	0	Not applicable.
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 June 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes