EMA/465362/2018

European Medicines Agency decision

P/0209/2018

of 17 July 2018

on the agreement of a paediatric investigation plan and on the granting of a waiver for palbociclib, (Ibrance), (EMEA-002146-PIP01-17) 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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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 application submitted by Pfizer Limited on 12 May 2017 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 1 June 2018, in accordance with Article 17 of Regulation (EC) No 1901/2006 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 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 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 palbociclib, (Ibrance), capsule, hard, age-appropriate oral dosage form, oral 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 waiver for palbociclib, (Ibrance), capsule, hard, age-appropriate oral dosage form, oral 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

This decision is addressed to Pfizer Limited, Ramsgate Road, CT13 9NJ - Sandwich, United Kingdom.

EMA/PDCO/166945/2018
London, 1 June 2018

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

EMEA-002146-PIP01-17

Scope of the application

Active substance(s):

Palbociclib

Invented name:

Ibrance

Condition(s):

Treatment of Ewing sarcoma

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Pfizer Limited

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, Pfizer Limited submitted for agreement to the European Medicines Agency on 12 May 2017 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 20 June 2017.

Supplementary information was provided by the applicant on 8 March 2018. The applicant proposed modifications to the paediatric investigation plan.

A meeting with the Paediatric Committee took place on 31 May 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 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 Ewing sarcoma

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- capsule, hard, oral use; age-appropriate oral dosage form, oral use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of Ewing sarcoma

2.1.1. Indication(s) targeted by the PIP

In combination with temozolomide and irinotecan for the treatment of patients from 2 years to less than 18 years of age with refractory or recurrent Ewing sarcoma

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

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

- Capsule, hard
- Age-appropriate oral dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an oral solution formulation for paediatric patients unable to swallow the capsules
Non-clinical studies	2	**Study 2** In *vivo* study to assess the anti-tumour activity of palbociclib used in combination with irinotecan and temozolomide compared irinotecan and temozolomide alone in Ewing sarcoma xenografts

		Study 3 In *vitro* study to evaluate the anti-tumour activity of palbociclib used in with irinotecan in Ewing sarcoma (EWS) cell lines
Clinical studies	2	**Study 4** Open-label, single-arm dose-escalation trial to evaluate the safety, pharmacokinetics and anti-tumour activity of palbociclib used in combination with temozolomide and irinotecan in children from 2 to less than 18 years of age (and young adults) with a recurrent or refractory solid tumour with a dose-finding phase (dose-escalation part) and an expansion cohort (dose expansion part) (Study A5481092) **Study 5** Open-label, randomised controlled trial to evaluate the efficacy, safety and pharmacokinetics of palbociclib used in combination with temozolomide and irinotecan as compared to temozolomide and irinotecan alone in children from 4 years to less than 18 years of age (and adults) with recurrent and /or refractory Ewing sarcoma (Study rEECur, palbociclib in combination with temozolomide and irinotecan arm)
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 2023
Deferral for one or more measures contained in the paediatric investigation plan:	No

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of breast carcinoma

Authorised indication(s):

- IBRANCE is indicated for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer:
  - in combination with an aromatase inhibitor;
  - in combination with fulvestrant in women who have received prior endocrine therapy.

In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist.

Authorised pharmaceutical form(s):

Capsule, hard

Authorised route(s) of administration:

Oral use