EMA/533513/2021

European Medicines Agency decision

P/0439/2021

of 29 October 2021

on the acceptance of a modification of an agreed paediatric investigation plan for abemaciclib (Verzenios), (EMEA-002342-PIP02-18-M01) 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/0021/2020 issued on 6 January 2020,

Having regard to the application submitted by Eli Lilly and Company Limited on 28 May 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 10 September 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.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[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 abemaciclib (Verzenios), film-coated tablet, age-appropriate oral solid dosage form, oral use, gastric use, 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 Eli Lilly and Company Limited, 8 Arlington Square West, Downshire Way, RG12 1PU – Bracknell, United Kingdom.

EMA/PDCO/330799/2021
Amsterdam, 10 September 2021

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

EMEA-002342-PIP02-18-M01

Scope of the application

Active substance(s):

Abemaciclib

Invented name:

Verzenios

Condition(s):

Treatment of glioma

Treatment of neuroblastoma

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

Eli Lilly and Company Limited

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Eli Lilly and Company Limited submitted to the European Medicines Agency on 28 May 2021 an application for modification of the agreed paediatric investigation plan as set out in the European Medicines Agency's decision P/0021/2020 issued on 6 January 2020.

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

The procedure started on 12 July 2021.

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 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 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

Not applicable.

2. Paediatric investigation plan

2.1. Condition:

Treatment of glioma

2.1.1. Indication(s) targeted by the PIP

Treatment of newly diagnosed patients with high-grade glioma

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate oral solid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of an age-appropriate film-coated tablet. **Study 2** Development of an age-appropriate oral solid dosage form.
Non-clinical studies	1	**Study 3** Juvenile toxicity study to assess potential brain and pancreas toxicity of abemaciclib following repeated dosing to juvenile rats. (Juvenile toxicity study).

Clinical studies	2	**Study 4** Open label, dose escalation trial to evaluate pharmacokinetics, safety and tolerability of abemaciclib in combination with irinotecan and temozolomide (triplet combination) and abemaciclib in combination with temozolomide (doublet combination) in children less than 18 years of age and weighing at least 10 kg and with BSA at least 0.5 m2 (and adults) with relapsed or refractory solid tumours. (Dose Escalation study). **Study 5** Open label, randomised, controlled study to evaluate safety and efficacy of abemaciclib in combination with temozolomide, compared to temozolomide monotherapy, in children from birth to less than 18 years of age (and adults) with newly diagnosed high-grade glioma (HGG). (Newly diagnosed HGG).
Extrapolation, modelling and simulation studies	1	**Study 6** Modelling and simulation study to develop a mechanistic population PK model to define PK parameters of the product in children from birth to less than 18 years of age.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition:

Treatment of neuroblastoma

2.2.1. Indication(s) targeted by the PIP

Treatment of relapsed/refractory neuroblastoma

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

From birth to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate oral solid dosage form

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Same as for condition treatment of glioma. **Study 2** Same as for condition Treatment of glioma.
Non-clinical studies	1	**Study 3** Same as for condition treatment of glioma.
Clinical studies	2	**Study 4** Same as for condition treatment of glioma. **Study 7** Open label, randomised, controlled study to evaluate safety and efficacy of abemaciclib in combination with temozolomide, compared to temozolomide plus irinotecan, in children from birth to less than 18 years of age (and adults) with relapsed/refractory neuroblastoma (NBL). (Relapsed/refractory NBL).
Extrapolation, modelling and simulation studies	1	**Study 6** Same as for condition treatment of glioma.
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 2028.
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 cancer

Authorised indication(s):

- Treatment of women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have received prior endocrine therapy. In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use