EMA/137677/2024

European Medicines Agency decision

P/0090/2024

of 12 April 2024

on the agreement of a paediatric investigation plan for alpelisib (Piqray), (EMEA-002016-PIP05-23) 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 application submitted by Novartis Europharm Limited on 14 April 2023 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 23 February 2024, in accordance with Article 17 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 agreement of a paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

[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

A paediatric investigation plan for alpelisib (Piqray), film-coated tablet, age-appropriate formulation, 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

This decision is addressed to Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, D04 A9N6 – Dublin, Ireland.

EMA/PDCO/538002/2023
Amsterdam, 23 February 2024

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

EMEA-002016-PIP05-23

Scope of the application

Active substance(s):

Alpelisib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of lymphatic malformations associated with a PIK3CA mutation

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Novartis Europharm Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted for agreement to the European Medicines Agency on 14 April 2023 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 22 May 2023.

Supplementary information was provided by the applicant on 31 October 2023. The applicant proposed modifications to the paediatric investigation planand and withdrew its request for a waiver.

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.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 lymphatic malformations associated with a PIK3CA mutation

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with lymphatic malformations associated with a PIK3CA mutation who require systemic therapy

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 formulation

2.1.4. Measures

Area	**Description**
Quality-related studies	**Study 1** Development of an age-appropriate formulation for oral use
Non-clinical studies	**Study 2** Juvenile animal study
Clinical studies	**Study 3 (CBYL719P12201)** Two-stage double-blind, randomised, placebo-controlled trial to evaluate pharmacokinetics, safety, efficacy of alpelisib in children from 6 to less than 18 years of age (and adults) with lymphatic malformations (LyM), with an open label non-comparative cohort in children from birth to less than 6 years of age to evaluate pharmacokinetics, safety, activity, and acceptability/palatability of the age-appropriate formulation developed in study 1
Modelling and simulation analyses	**Study 4** Modelling and simulation analyses to support dose determination in children from birth to less than 18 years of age with lymphatic malformations.

Other studies	Not applicable
Extrapolation plan	Studies 3 and 4 are part of an extrapolation plan covering the paediatric population from birth to less than 18 years of age, as agreed by the PDCO.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By April 2028
Deferral for one or more measures contained in the paediatric investigation plan:	No

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of breast cancer

Authorised indication(s):

- Piqray is indicated in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with a PIK3CA mutation after disease progression following endocrine therapy as monotherapy.
  - Invented name(s): Piqray
  - Authorised pharmaceutical form(s): Film-coated tablet
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure