EMA/776062/2022

European Medicines Agency decision

P/0412/2022

of 30 September 2022

on the acceptance of a modification of an agreed paediatric investigation plan for alpelisib (Piqray and associated names), (EMEA-002016-PIP03-19-M02) 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.

European Medicines Agency decision

P/0412/2022

of 30 September 2022

on the acceptance of a modification of an agreed paediatric investigation plan for alpelisib (Piqray and associated names), (EMEA-002016-PIP03-19-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 European Medicines Agency's decision P/0329/2020 issued on 17 August 2020 and the decision P/0536/2021 issued on 3 December 2021,

Having regard to the application submitted by Novartis Europharm Limited on 27 May 2022 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 9 September 2022, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for alpelisib (Piqray and associated names), film-coated tablet, granules, oral 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 Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, 4 – Dublin, Ireland.

EMA/PDCO/566973/2022
Amsterdam, 9 September 2022

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

EMEA-002016-PIP03-19-M02

Scope of the application

Active substance(s):

Alpelisib

Invented name:

Piqray (and associated names)

Condition(s):

Treatment of PIK3CA related overgrowth spectrum

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Granules

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Novartis Europharm 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, Novartis Europharm Limited submitted to the European Medicines Agency on 27 May 2022 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/0329/2020 issued on 17 August 2020 and the decision P/0536/2021 issued on 3 December 2021.

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

The procedure started on 11 July 2022.

Scope of the modification

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

2. The measures and timelines of the paediatric investigation plan and the subset of the paediatric population and condition 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 (Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha) PIK3CA related overgrowth spectrum

The waiver applies to:

- the paediatric population from birth to less than 2 years;
- film-coated tablet and granules, 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 PIK3CA related overgrowth spectrum

2.1.1. Indication(s) targeted by the PIP

Treatment of PIK3CA related overgrowth spectrum (PROS)

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

From 2 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Granules

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of granules for the paediatric population from 2 to less than 6 years of age and for those not able to use the film-coated tablets.
Non-clinical studies	Not applicable
Clinical studies	**Study 2** Efficacy, safety and pharmacokinetics double-blind randomized, placebo-controlled study of alpelisib in (adults and) paediatric patients from 2 to less than 18 years of age with PROS.

Extrapolation, modelling and simulation studies	**Study 3** Modelling and simulation study for establishing the appropriate dose of alpelisib of granule formulation in paediatric patients from 2 to less than 6 years of age.
Other studies	**Study 4** Site-based retrospective, non-interventional chart review study of paediatric (and adult) male and female patients with PIK3CA related overgrowth spectrum (PROS) to assess changes in clinical and functional outcomes as well as safety in patients with PROS treated with alpelisib.
Other measures	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 2027
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):

Condition:

1. Treatment of breast cancer

Authorised indication:

- 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.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use