EMA/627442/2021

European Medicines Agency decision

P/0476/2021

of 3 December 2021

on the acceptance of a modification of an agreed paediatric investigation plan for vericiguat (Verguvo), (EMEA-001636-PIP01-14-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.

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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/0126/2015 issued on 5 June 2015, and decision P/0070/2017 issued on 17 March 2017,

Having regard to the application submitted by Bayer AG on 9 July 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and proposing a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 15 October 2021, in accordance with Article 22 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 acceptance of changes to the agreed paediatric investigation plan and to the deferral and on the granting of a waiver.

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

(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

Changes to the agreed paediatric investigation plan for vericiguat (Verguvo), age-appropriate oral liquid dosage form, tablet, oral use, including changes to the deferral, 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

A waiver for vericiguat (Verguvo), age-appropriate oral liquid dosage form, tablet, 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 Bayer AG, Kaiser-Wilhelm-Allee 1, 51368 Leverkusen, Germany.

EMA/PDCO/404403/2021
Amsterdam, 15 October 2021

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

EMEA-001636-PIP01-14-M02

Scope of the application

Active substance(s):

Vericiguat

Invented name:

Verquvo

Condition(s):

Treatment of left ventricular failure

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Age-appropriate oral liquid dosage form

Tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Bayer AG

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bayer AG submitted to the European Medicines Agency on 9 July 2021 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's P/0126/2015 issued on 5 June 2015, and decision P/0070/2017 issued on 17 March 2017.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral and proposed a waiver.

The procedure started on 17 August 2021.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. A waiver for a paediatric subset has been added and the deferral removed.

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 and to the deferral in the scope set out in the Annex I of this opinion;
   - to grant a waiver for one or more subsets of the paediatric population concluded in accordance with Article 11(1)(c) of Regulation (EC) No 1901/2006 as amended, 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 paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in 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 left ventricular failure

The waiver applies to:

- the paediatric population from birth to 28 days of age;
- age-appropriate oral liquid dosage form and tablet, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition

Treatment of left ventricular failure

2.1.1. Indication(s) targeted by the PIP

Treatment of symptomatic chronic heart failure with systemic left ventricular systolic dysfunction in paediatric patients > 28 days to < 18 years of age. Vericiguat reduces N-terminal pro-hormone B-type natriuretic peptide (NT-proBNP) and is expected to improve cardiovascular outcomes.

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

From greater than 28 days to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Tablet

Age-appropriate oral liquid formulation

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of new age-appropriate oral liquid dosage form.
Non-clinical studies	2	**Study 2** Establishment of dose levels for definite juvenile toxicity study in rats (4-weeks study).

		Study 3 Evaluation of systemic toxicity of vericiguat in juvenile rats (13-weeks study).
Clinical studies	3	**Study 4** Deleted in EMEA-001636-PIP01-14-M02 **Study 5** Deleted in EMEA-001636-PIP01-14-M02 **Study 6** Relative bioavailability and food effect study in adult healthy subjects. **Study 8** (added in EMEA-001636-PIP01-14-M02) Randomised placebo-controlled, double-blind multi-centre, adaptive, seamless trial to evaluate the safety, efficacy, and pharmacokinetics of vericiguat in paediatric participants from greater than 28 days to less than 18 years of age with symptomatic chronic heart failure due to left ventricular systolic dysfunction **Study 9** (added in EMEA-001636-PIP01-14-M02) Relative bioavailability and food effect study in adult healthy subjects of the oral liquid formulation
Extrapolation, modelling and simulation studies	1	**Study 7** PBPK modelling study to predict the PK properties in the paediatric population.
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:	No
Date of completion of the paediatric investigation plan:	By October 2029
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 left ventricular failure

Authorised indication(s):

- Treatment of symptomatic chronic heart failure in adult patients with reduced ejection fraction who are stabilised after a recent decompensation event requiring IV therapy

Authorised pharmaceutical form(s):

Film-coated tablets

Authorised route(s) of administration:

Oral use