EMA/137674/2024

European Medicines Agency decision

P/0092/2024

of 12 April 2024

on the acceptance of a modification of an agreed paediatric investigation plan for milvexian (EMEA-003220-PIP01-22-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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on the acceptance of a modification of an agreed paediatric investigation plan for milvexian (EMEA-003220-PIP01-22-M01) 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/0274/2023 issued on 7 August 2023,

Having regard to the application submitted by Janssen-Cilag International N.V. on 17 November 2023 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 23 February 2024, 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 milvexian, film-coated tablet, age-appropriate oral dosage form, 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 Janssen-Cilag International N.V., Turnhoutseweg 30, 2340 - Beerse, Belgium.

EMA/PDCO/537991/2023 Corr
Amsterdam, 23 February 2024

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

EMEA-003220-PIP01-22-M01

Scope of the application

Active substance(s):

Milvexian

Invented name and authorisation status:

See Annex II

Condition(s):

Prevention of thromboembolism in patients with cardiovascular diseases

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Janssen-Cilag International N.V.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Janssen-Cilag International N.V. submitted to the European Medicines Agency on 17 November 2023 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/0274/2023 issued on 7 August 2023.

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

The procedure started on 3 January 2024.

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(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:

Prevention of thromboembolism in patients with cardiovascular diseases

The waiver applies to:

- preterm and term newborn infants from birth to less than 28 days of age;
- film-coated tablet, age-appropriate oral dosage form, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric investigation plan

2.1. Condition:

Prevention of thromboembolism in patients with cardiovascular diseases

2.1.1. Indication(s) targeted by the PIP

Primary prevention of thromboembolic events in paediatric patients from 28 days to less than 18 years of age with congenital heart disease

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

From 28 days to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet, age-appropriate oral dosage form

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age-appropriate oral solid formulation.
Non-clinical studies	**Study 2** In vitro assessment of coagulation assays in paediatric plasma samples spiked with milvexian. **Study 3** Reproductive toxicity animal study to assess potential effects of milvexian on pregnant/lactating rabbits and postnatal development of the offspring.

Clinical studies	**Study 4** Open-label, single dose trial to evaluate pharmacokinetics, safety, tolerability, acceptability, and palatability of milvexian in children from 28 days to less than 18 years of age at risk of thromboembolic events. **Study 5** Open-label, randomised, multiple dose trial to evaluate pharmacokinetics, safety, and efficacy of milvexian compared to best standard of care in children from 28 days to less than 18 years of age with congenital heart disease at risk of thromboembolic events.
Modelling and simulation studies	**Study 6** Modelling and simulation study to inform the dose and treatment regimen in studies 4 and 5, to achive comparable drug exposure between adult and paediatric populations and characterize PK/PD relationships.
Other studies	Not applicable.
Extrapolation plan	Studies 4, 5, 6 are part of an extrapolation plan covering the paediatric population from 28 days 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 June 2032
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.