EMA/517374/2023

European Medicines Agency decision

P/0488/2023

of 4 December 2023

on the acceptance of a modification of an agreed paediatric investigation plan for maralixibat chloride (Livmarli), (EMEA-001475-PIP03-17-M04) 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 European Medicines Agency's decision P/0024/2018 issued on 30 January 2018, the decision P/0409/2019 issued on 6 December 2019, the decision P/0200/2020 issued on 25 May 2020 and the decision P/0436/2022 issued on 28 October 2022,

Having regard to the application submitted by Mirum Pharmaceuticals on 3 July 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 13 October 2023, 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 maralixibat chloride (Livmarli), oral solution, tablet, 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 covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0149/2015 issued on 10 July 2015, including subsequent modifications thereof.

Article 3

This decision is addressed to Mirum Pharmaceuticals, 950 Tower Lane, Suite 1050, CA 94404 - Foster City, United States.

EMA/PDCO/323430/2023
Amsterdam, 13 October 2023

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

EMEA-001475-PIP03-17-M04

Scope of the application

Active substance(s):

Maralixibat chloride

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of progressive familial intrahepatic cholestasis

Pharmaceutical form(s):

Oral solution

Tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Mirum Pharmaceuticals

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Mirum Pharmaceuticals submitted to the European Medicines Agency on 3 July 2023 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0024/2018 issued on 30 January 2018, the decision P/0409/2019 issued on 6 December 2019, the decision P/0200/2020 issued on 25 May 2020 and the decision P/0436/2022 issued on 28 October 2022.

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

The procedure started on 14 August 2023.

Scope of the modification

A new pharmaceutical form was added.

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

Not applicable.

2. Paediatric investigation plan

2.1. Condition:

Treatment of progressive familial intrahepatic cholestasis (PFIC)

2.1.1. Indication(s) targeted by the PIP

Treatment of pruritus in progressive familial intrahepatic cholestasis

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)

Oral solution

Tablet

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable.
Non-clinical studies	Not applicable.
Clinical studies	**Study 1 (MRX-502)** Randomised, double-blind, placebo-controlled study in children from 12 months to less than 18 years of age with PFIC. **Study 2 (LUM001-501)** Open label safety and efficacy study in children from 12 months to less than 18 years of age with PFIC1 or 2. **Study 3 (MRX-801)** *(study added during procedure EMEA-001475-PIP03-17-M01)* Open-label, uncontrolled safety study to evaluate the safety and tolerability of Maralixibat in paediatric subjects with cholestatic liver diseases including, but not limited to, Alagille Syndrome and PFIC from birth to less than 12 months of age.
Extrapolation, modelling and simulation studies	Not applicable.

Other studies	Not applicable.
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:	No.
Date of completion of the paediatric investigation plan:	By December 2023.
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:

Condition(s) and authorised indication(s)

1. Treatment of Alagille syndrome

Authorised indication(s):

- Livmarli is indicated for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 2 months of age and older
  - Invented name(s): Livmarli.
  - Authorised pharmaceutical form(s): Oral solution.
  - Authorised route(s) of administration: Oral use.
  - Authorised via centralised procedure