EMA/668766/2022

European Medicines Agency decision

P/0298/2022

of 10 August 2022

on the acceptance of a modification of an agreed paediatric investigation plan for maralixibat chloride (EMEA-001475-PIP02-13-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 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/0149/2015 issued on 10 July 2015 and the decision P/0133/2021 issued on 14 April 2021,

Having regard to the application submitted by Mirum Pharmaceuticals on 18 March 2022 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 24 June 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 maralixibat chloride, 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 is addressed to Mirum Pharmaceuticals, 950 Tower Lane, Suite 1050, CA 94404 - Foster City, United States.

EMA/PDCO/180748/2022
Amsterdam, 24 June 2022

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

EMEA-001475-PIP02-13-M02

Scope of the application

Active substance(s):

Maralixibat chloride

Condition(s):

Treatment of Alagille syndrome

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 18 March 2022 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0149/2015 issued on 10 July 2015 and the decision P/0133/2021 issued on 14 April 2021.

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

The procedure started on 25 April 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 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 annex 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 Alagille syndrome

2.1.1. Indication(s) targeted by the PIP

Treatment of Alagille syndrome (ALGS)

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	**Study 1 (2939-001/MRXNC-001)** Juvenile toxicity study in rats
Clinical studies	**Study 2 (LUM001-302)** Randomised double-blind, placebo controlled safety and efficacy study of maralixibat in children 12 months to 18 years of age with Alagille syndrome **Study 3 (LUM001-301)** Randomised double-blind, placebo controlled safety and efficacy study of maralixibat in children 12 months to 18 years of age with Alagille syndrome **Study 4 (LUM001-304)** Open label with a double-blind placebo controlled randomised drug withdrawal period, safety and efficacy study maralixibat in children 12 months to 18 years of age with Alagille syndrome **Study 5 (MRX-801)** Open-label, uncontrolled safety study to evaluate the safety and tolerability of maralixibat in paediatric subjects from birth to less

	than 12 months of age with cholestatic liver diseases due to Alagille syndrome (ALGS) and progressive familial intrahepatic cholestasis (PFIC)
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:	Yes
Date of completion of the paediatric investigation plan:	By December 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes