EMA/291603/2024

European Medicines Agency decision

P/0230/2024

of 19 July 2024

on the acceptance of a modification of an agreed paediatric investigation plan for ralinepag (EMEA-002432-PIP02-20-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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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/0244/2021 issued on 9 July 2021,

Having regard to the application submitted by United Therapeutics Corporation on 26 February 2024 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 31 May 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 and to the deferral.

(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.

[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 ralinepag, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, oral use, enteral 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

This decision is addressed to United Therapeutics Corporation, 55 TW Alexander Drive, 27709 - Research Triangle Park, USA.

EMA/PDCO/90773/2024
Amsterdam, 31 May 2024

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

EMEA-002432-PIP02-20-M01

Scope of the application

Active substance(s):

Ralinepag

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of pulmonary arterial hypertension

Pharmaceutical form(s):

Age-appropriate oral solid dosage form

Age-appropriate oral liquid dosage form

Route(s) of administration:

Oral use

Enteral use

Name/corporate name of the PIP applicant:

United Therapeutics Corporation

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, United Therapeutics Corporation submitted to the European Medicines Agency on 26 February 2024 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/0244/2021 issued on 9 July 2021.

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

The procedure started on 2 April 2024.

Scope of the modification

Some timelines 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 and to the deferral in the scope set out in the Annex I of this opinion.
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:

Treatment of pulmonary arterial hypertension (PAH)

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form; oral use, enteral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition:

Treatment of pulmonary arterial hypertension

2.1.1. Indication(s) targeted by the PIP

Treatment of WHO Group I PAH to improve exercise capacity and to delay clinical worsening in children from 1 year to less than 18 years of age

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

From 1 year to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Age-appropriate oral solid dosage form

Age-appropriate oral liquid dosage form

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1 (ADP811-FD01)** Development of an age-appropriate oral solid dosage form **Study 2 (ADP811-FD02)** Development of an age-appropriate oral liquid dosage form
Non-clinical studies	**Study 3 (APD811-JAS01)** Juvenile dose-finding toxicity study in rats **Study 4 (APD811-JAS02)** Juvenile toxicity study in rats

Clinical studies	**Study 5 (ROR-PH-201)** Open-label single-arm study to investigate the pharmacokinetics (PK), safety, tolerability and pharmacodynamics (PD) of ralinepag in paediatric patients from 1 year to less than 18 years of age with PAH.
Extrapolation, modelling and simulation studies	**Study 6 (ROR-PH-201-MS)** Population PK/PD analysis to determine paediatric dosing and support extrapolation of efficacy for ralinepag in children from 1 year to less than 18 years of age from adults. **Study 7 (ROR-PH-201-EX)** Analysis of existing in house and literature data on exposure-response relationships of ralinepag and compounds with a similar mode of action for the treatment of PAH to support extrapolation of efficacy from adults to paediatric patients from 1 year to less than 18 years of age with PAH.
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 June 2028
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.