

EMA/318092/2021

European Medicines Agency decision P/0244/2021

of 9 July 2021

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for ralinepag (EMEA-002432-PIP02-20) 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 726/2004¹,

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 Agency²,

Having regard to the application submitted by United Therapeutics Corporation on 06 July 2020 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 May 2021, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation 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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.
- (2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.
- (3) It is therefore appropriate to adopt a decision granting a deferral.
- (4) 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

A paediatric investigation plan for ralinepag, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, oral use, enteral 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 agreed.

Article 2

A deferral for ralinepag, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, oral use, enteral 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

A waiver for ralinepag, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, oral use, enteral 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 4

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

EMA/PDCO/132375/2021
Amsterdam, 21 May 2021

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMA-002432-PIP02-20

Scope of the application

Active substance(s):

Ralinepag

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 16(1) of Regulation (EC) No 1901/2006 as amended, United Therapeutics Corporation submitted for agreement to the European Medicines Agency on 6 July 2020 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 18 August 2020.

Supplementary information was provided by the applicant on 3 February 2021. The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:
 - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
 - to grant a deferral in accordance with Article 21 of said Regulation;
 - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 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

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	Number of measures	Description
Quality-related studies	2	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	2	Study 3 (APD811-JAS01)

		Juvenile dose-finding toxicity study in rats Study 4 (APD811-JAS02) Juvenile toxicity study in rats
Clinical studies	1	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	2	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	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 June 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes