EMA/75565/2018

European Medicines Agency decision

P/0085/2018

of 16 March 2018

on the acceptance of a modification of an agreed paediatric investigation plan for rolapitant (Varuby), (EMEA-001768-PIP02-15-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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

European Medicines Agency decision

P/0085/2018

of 16 March 2018

on the acceptance of a modification of an agreed paediatric investigation plan for rolapitant (Varuby), (EMEA-001768-PIP02-15-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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0047/2016 issued on 3 March 2016,

Having regard to the application submitted by Tesaro UK Ltd on 6 November 2017 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 26 January 2018, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for rolapitant (Varuby), tablet, age-appropriate oral dosage form, oral 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 Tesaro UK Ltd, 55 Baker Street, W1U 7EU - London, United Kingdom.

EMA/PDCO/736535/2017
London, 26 January 2018

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

EMEA-001768-PIP02-15-M01

Scope of the application

Active substance(s):

Rolapitant

Invented name:

Varuby

Condition(s):

Prevention of nausea and vomiting

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Tablet

Age-appropriate oral dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

TESARO UK Ltd

Information about the authorised medicinal product:

See Annex II

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, TESARO UK Ltd submitted to the European Medicines Agency on 6 November 2017 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/0047/2016 issued on 3 March 2016.

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

The procedure started on 28 November 2017.

Scope of the modification

Some measures and 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.

   The Icelandic Paediatric Committee member 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

Prevention of nausea and vomiting

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- tablet, age-appropriate oral dosage form, for oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition

Prevention of nausea and vomiting

2.1.1. Indication(s) targeted by the PIP

Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cisplatin-based cancer therapy and moderately emetogenic cancer therapy

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

From 6 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Tablet, age-appropriate oral dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate oral dosage form.
Non-clinical studies	1	**Study 2** Definitive juvenile toxicity study. **Study 8** (Study added in procedure EMEA-001768-PIP02-15-M01) Age cohort juvenile toxicology study.
Clinical studies	4	**Study 3** Multicenter, open-label single dose study to evaluate the safety/tolerability and pharmacokinetic of rolapitant (part 1) followed by a randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of rolapitant compared to placebo as adjunct treatment to 5-HT3 receptor antagonists and dexamethasone in the

		prevention of nausea and vomiting (part 2) in paediatric patients from 12 to less than 18 years of age receiving highly emetogenic chemotherapy and moderately emetogenic chemotherapy treatment. **Study 4** Multicenter, open-label dose-ranging multi-cohort study to evaluate the safety/tolerability and pharmacokinetic of rolapitant in paediatric patients from 6 months to less than 12 years of age receiving highly emetogenic chemotherapy and moderately emetogenic chemotherapy treatment. **Study 5** Randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of rolapitant compared to placebo as adjunct treatment to 5-HT3 receptor antagonists and dexamethasone in the prevention of nausea and vomiting in paediatric patients from 6 months to less than 12 years of age receiving highly emetogenic chemotherapy and moderately emetogenic chemotherapy treatment. **Study 6** Single dose study comparing rolapitant tablets (reference) and age-appropriate oral liquid formulation (test) to evaluate the bioavailability between the two formulations in healthy adult subjects.
Extrapolation, modelling and simulation studies	1	**Study 7** Modelling and simulation study to evaluate the use and support dosing regimen of rolapitant in the prevention of nausea and vomiting in paediatric patients from 6 months to less than 18 years of age receiving highly emetogenic chemotherapy and moderately emetogenic chemotherapy treatment.
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 March 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

Prevention of nausea and vomitingAuthorised indication(s):

Prevention of delayed nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy in adults. Varuby is given as part of combination therapy

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use