EMA/381968/2018

# European Medicines Agency decision

P/0168/2018

of 18 June 2018

on the acceptance of a modification of an agreed paediatric investigation plan for betrixaban (EMEA-001834-PIP02-16-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 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/0352/2016 issued on 2 December 2016,

Having regard to the application submitted by Portola Pharma UK Limited on 3 February 2018 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 27 April 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.

(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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

***Article 1***

Changes to the agreed paediatric investigation plan for betrixaban, capsule, hard, age appropriate oral liquid dosage form, 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 Portola Pharma UK Limited, 209 Tower Bridge Business Centre, 46-48 East Smithfield, E1W 1AW - London, United Kingdom.

EMA/PDCO/92903/2018
London, 27 April 2018

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

EMEA-001834-PIP02-16-M01

## Scope of the application

**Active substance(s):**

Betrixaban

**Condition(s):**

Prevention of venous thromboembolism

**Pharmaceutical form(s):**

Capsule, hard

Age appropriate oral liquid dosage form

**Route(s) of administration:**

Oral use

**Name/corporate name of the PIP applicant:**

Portola Pharma UK Limited

## Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Portola Pharma UK Limited submitted to the European Medicines Agency on 3 February 2018 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0352/2016 issued on 2 December 2016.

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

The procedure started on 27 February 2018.

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## Scope of the modification

A timeline of the Paediatric Investigation Plan has 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 Norwegian Paediatric Committee member 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*

Prevention of venous thromboembolism

### 2.1.1. Indication(s) targeted by the PIP

Prophylaxis of venous thromboembolism in paediatric patients

### 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)

Capsule, hard

Age appropriate oral liquid dosage form

### 2.1.4. Measures

| Area | Number of measures | Description |
|---|---|---|
| **Quality-related studies** | 1 | Study 1<br>Development of an age-appropriate oral liquid dosage form. |
| **Non-clinical studies** | 1 | Study 2<br>Study with rats to investigate potential adverse effects on the kidneys, liver, bladder and eye. |
| **Clinical studies** | 4 | Study 3<br>Single dose PK (pharmacokinetic) study in paediatric patients who completed a course of anticoagulation, from 28 days to less than 18 years old in the fed or fasted state.<br>Study 4<br>Single arm open label study in paediatric patients from 28 days to less than 18 years old with an acute medical or surgical illness who require prophylaxis of venous thromboembolism with low intensity anticoagulation. |

| | | |
|---|---|---|
| | | Study 5<br><br>Single arm, open label, PK, safety and activity study in term and preterm neonates (less than 28 days) with an umbilical venous or umbilical arterial catheter who require prophylaxis of venous thromboembolism with low intensity anticoagulation.<br><br>Study 6<br><br>Open label, single dose trial to evaluate PK/PD of andexanet alfa in children administered at the end of their treatment with betrixaban.<br><br>*This study is the same as Study 6 in EMEA-001902-PIP01-15, P/0199/2016 of July 2016 and subsequent modifications thereof.* |
| **Extrapolation, modelling and simulation studies** | 2 | Study 7<br><br>Modelling and simulation sub-study 1 (as part of Study 4, Part 1 and Part 2)<br><br>Study 8<br><br>Modelling and simulation sub-study 2 (as part of Study 4, Part 1 and Part 2) |
| **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: | Yes |
| Date of completion of the paediatric investigation plan: | By December 2024. |
| Deferral for one or more measures contained in the paediatric investigation plan: | Yes |