EMA/479450/2016

European Medicines Agency decision

P/0199/2016

of 18 July 2016

on the agreement of a paediatric investigation plan and on the granting of a deferral for andexanet alfa (EMEA-001902-PIP01-15) 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 application submitted by Portola Pharma UK Limited on 23 November 2015 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 24 June 2016, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 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.

(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.

[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 andexanet alfa, powder for solution for infusion, intravenous 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 andexanet alfa, powder for solution for infusion, intravenous 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

This decision is addressed to Portola Pharma UK Limited, 209 Tower Bridge Business Centre, 46-48 East Smithfield, E1W 1AW – London, United Kingdom.

Done at London, 18 July 2016

For the European Medicines Agency
Zaïde Frias
Head of Division
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/257234/2016
London, 24 June 2016

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

EMEA-001902-PIP01-15

Scope of the application

Active substance(s):

Andexanet alfa

Condition(s):

Treatment of factor Xa inhibitor associated haemorrhage

Prevention of factor Xa inhibitor associated haemorrhage

Pharmaceutical form(s):

Powder for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Portola Pharma UK Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Portola Pharma UK Limited submitted for agreement to the European Medicines Agency on 23 November 2015 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 4 January 2016.

Supplementary information was provided by the applicant on 4 April 2016. The applicant proposed modifications to the paediatric investigation plan.

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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 18 of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

   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 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 factor Xa inhibitor associated haemorrhage

2.1.1. Indication(s) targeted by the PIP

For the reversal of anticoagulation due to direct and indirect factor Xa inhibitors in patients experiencing an acute major bleeding event.

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)

Intravenous use

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of appropriately sized vials to cover all the paediatric population.
Non-clinical studies	0	Not applicable.
Clinical studies	5	**Study 2** Open label, single dose trial to evaluate PK/PD of andexanet alfa in children from birth to less than 18 years of age, administered at the end of their treatment with enoxaparin. **Study 3** Open label, single dose trial to evaluate PK/PD of andexanet alfa in children from birth to less than 18 years of age, administered at the end of their treatment with rivaroxaban. **Study 4** Open label, single dose trial to evaluate PK/PD of andexanet alfa in children from birth to less than 18 years of age, administered at the end of their treatment with apixaban.

Area	Number of measures	Description
		Study 5 Open label, single dose trial to evaluate PK/PD of andexanet alfa in children from birth to less than 18 years of age, administered at the end of their treatment with edoxaban. **Study 6** Open label, single dose trial to evaluate PK/PD of andexanet alfa in children from birth to less than 18 years of age, administered at the end of their treatment with betrixaban.
Extrapolation, modelling and simulation studies	1	**Study 7** A population PK/PD model for the determination of andexanet dose and rate of infusion required for reversal of anticoagulation, for direct and indirect fXa inhibitors in paediatric populations.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition

Prevention of factor Xa inhibitor associated haemorrhage

2.2.1. Indication(s) targeted by the PIP

For the reversal of anticoagulation due to direct and indirect factor Xa inhibitors in patients requiring urgent surgery

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

From birth to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Intravenous use

2.2.4. Measures

The same as measures for condition "Treatment of factor Xa inhibitor associated haemorrhage".

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 January 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes