EMA/415148/2020

European Medicines Agency decision

P/0349/2020

of 9 September 2020

on the acceptance of a modification of an agreed paediatric investigation plan for andexanet alfa (Ondexxya), (EMEA-001902-PIP01-15-M04) 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/0199/2016 issued on 18 July 2016, the decision P/0307/2017 issued on 30 October 2017, the decision P/0120/2018 issued on 11 April 2018 and the decision P/0243/2018 issued on 15 August 2018,

Having regard to the application submitted by Portola Netherlands B.V. on 17 April 2020 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 24 July 2020, 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 andexanet alfa (Ondexxya), powder for solution for infusion, intravenous 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 Netherlands B.V., Prins Bernhardplein 200, 1097 JB - Amsterdam, The Netherlands.

EMA/PDCO/232920/2020
Amsterdam, 24 July 2020

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

EMEA-001902-PIP01-15-M04

Scope of the application

Active substance(s):

Andexanet alfa

Invented name:

Ondexxya

Condition(s):

Treatment of factor Xa inhibitor associated haemorrhage

Prevention of factor Xa inhibitor associated haemorrhage

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Powder for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Portola Netherlands B.V.

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Portola Netherlands B.V. submitted to the European Medicines Agency on 17 April 2020 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0199/2016 issued on 18 July 2016, the decision P/0307/2017 issued on 30 October 2017, the decision P/0120/2018 issued on 11 April 2018 and the decision P/0243/2018 issued on 15 August 2018.

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

The procedure started on 26 May 2020.

Scope of the modification

Some measures 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 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 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

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	4	**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

		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*** *removed from PIP during procedure EMEA-001902-PIP01-15-M04.*
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 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 March 2026
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 and treatment of factor Xa inhibitor associated haemorrhage

Authorised indication(s):

- For adult patients treated with a direct factor Xa (FXa) inhibitor (apixaban or rivaroxaban) when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding.

Authorised pharmaceutical form(s):

Powder for solution for infusion

Authorised route(s) of administration:

Intravenous use