EMA/471932/2021

European Medicines Agency decision

P/0397/2021

of 8 September 2021

on the acceptance of a modification of an agreed paediatric investigation plan for human fibrinogen / human thrombin (Evicel, Evarrest), (EMEA-001149-PIP01-11-M07) 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/0025/2012 issued on 27 January 2012, the decision P/0193/2012 issued on 24 August 2012, the decision P/0171/2015 issued on 7 August 2015, the decision P/0067/2016 issued on 18 March 2016, the decision P/0399/2017 issued on 19 December 2017, the decision P/0339/2019 issued on 10 September 2019 and the decision P/0051/2021 issued on 27 January 2021,

Having regard to the application submitted by Omrix Biopharmaceuticals N.V. on 19 April 2021 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 23 July 2021, 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 human fibrinogen / human thrombin (Evicel, Evarrest), solution for sealant, sealant matrix, epilesional 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 Omrix Biopharmaceuticals N.V., Leonardo da Vinci Laan 15, B-1831 - Diegem Belgium.

EMA/PDCO/253680/2021
Amsterdam, 23 July 2021

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

EMEA-001149-PIP01-11-M07

Scope of the application

Active substance(s):

Human fibrinogen / human thrombin

Invented name:

Evicel

Evarrest

Condition(s):

Treatment of haemorrhage resulting from a surgical procedure

Treatment of cerebrospinal fluid leakage resulting from a neurosurgical procedure

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for sealant

Sealant matrix

Route(s) of administration:

Epilesional use

Name/corporate name of the PIP applicant:

Omrix Biopharmaceuticals N.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, Omrix Biopharmaceuticals N.V. submitted to the European Medicines Agency on 19 April 2021 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/0025/2012 issued on 27 January 2012, the decision P/0193/2012 issued on 24 August 2012, the decision P/0171/2015 issued on 7 August 2015, the decision P/0067/2016 issued on 18 March 2016, the decision P/0399/2017 issued on 19 December 2017, the decision P/0339/2019 issued on 10 September 2019 and the decision P/0051/2021 issued on 27 January 2021.

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

The procedure started on 25 May 2021.

Scope of the modification

Some 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 Norwegian 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

1.1 Condition

Treatment of haemorrhage resulting from a surgical procedure

The waiver applies to:

- from birth to less than 28 days;
- sealant matrix, epilesional use;
- on the grounds that the specific medicinal product is likely to be ineffective.

2. Paediatric Investigation Plan

2.1. Condition

Treatment of haemorrhage resulting from a surgical procedure

2.1.1. Indication(s) targeted by the PIP

Indicated as supportive treatment in surgery, for improvement of haemostasis where standard surgical techniques are ineffective and impractical

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

From birth to less than 18 years of age (for solution for sealant)

From 28 days to less than 18 years of age (for sealant matrix)

2.1.3. Pharmaceutical form(s)

Solution for sealant

Sealant matrix

2.1.4. Measures

Area	**Number of studies**	**Description**
Quality-related studies	0	*Study 1* *Deleted in procedure EMEA-001149-PIP01-11-M02.*
Non-clinical studies	0	Not applicable.
Clinical studies	2	**Study 2 (EVARREST paediatric mild to moderate bleeding study)** Open-label, randomised, multicentre, active-controlled, trial to evaluate safety and efficacy of sealant matrix human fibrinogen / human thrombin as an adjunct to control mild to moderate

		bleeding in children from 1 month to less than 18 years of age requiring surgery. *Study 3* *Deleted in procedure EMEA-001149-PIP01-11-M05***.** **Study 4 (EVICEL paediatric bleeding study)** Open-label randomised, multicentre, active -controlled trial to evaluate safety and efficacy of human fibrinogen / human thrombin solution for sealant as an adjunct to control bleeding in children from birth to less than 18 years of age requiring surgery.

2.2. Condition

Treatment of cerebrospinal fluid leakage resulting from a neurosurgical procedure

2.2.1. Indication(s) targeted by the PIP

Indicated as supportive treatment in surgery, cerebrospinal leakage resulting from neurosurgical procedure

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)

Solution for sealant

2.2.4. Measures

Area	Number of studies	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 5 (EVICEL paediatric neurosurgery study)** A randomized, controlled clinical study evaluating the safety and efficacy of solution for sealant when used as an adjunct to dural sutures during neurosurgical procedures.

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 studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

Evicel

1. Treatment of haemorrhage resulting from a surgical procedure

Authorised indication(s):

- Supportive treatment in surgery where standard surgical techniques are insufficient, for improvement of haemostasis
- Suture support for haemostasis in vascular surgery.

2. Treatment of cerebrospinal fluid leakage resulting from a neurosurgical procedure

Authorised indication(s):

- Suture line sealing in dura mater closure

Authorised pharmaceutical form(s):

Solution for sealant

Authorised route(s) of administration:

Epilesional use