MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept changes to the agreed paediatric investigation plan and to the deferral

MHRA-100083-PIP01-21-M01

Scope of the Application

Active Substance(s)

Human Fibrinogen (INN) / Human Thrombin (INN) ; HUMAN FIBRINOGEN; HUMAN THROMBIN

Condition(s)

Treatment of: haemorrhage from a surgical procedure, CSF leakage from a neurosurgical procedure

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.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Omrix Biopharmaceuticals N.V. submitted to the licensing authority on 20/04/2021 18:53 BST an application for a Modification

The procedure started on 09/09/2021 08:09 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept changes to the agreed paediatric investigation plan and to the deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100083-PIP01-21-M01

Of 15/09/2021 09:36 BST

On the adopted decision for Human Fibrinogen (INN) / Human Thrombin (INN) ; HUMAN FIBRINOGEN; HUMAN THROMBIN (MHRA-100083-PIP01-21-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for Human Fibrinogen (INN) / Human Thrombin (INN) ; HUMAN FIBRINOGEN; HUMAN THROMBIN, Solution for sealant; Sealant matrix , Epilesional use .

This decision is addressed to Omrix Biopharmaceuticals N.V., Leonardo da Vinci Laan 15, Diegem, Belgium, B-1831

ANNEX I

1. Waiver

1.1 Condition:

Condition 1: Treatment of haemorrhage resulting from a surgical procedure The waiver applies / applied to: Paediatric Subset(s): all subsets of the paediatric population from birth to less than 28 days Pharmaceutical form(s): sealant matrix Route(s) of administration: Epilesional use; Reason for granting waiver: on the grounds that the specific medicinal product is likely to be ineffective. Condition 2 Treatment of cerebrospinal fluid leakage resulting from a neurosurgical procedure Pharmaceutical form(s): Solution for sealant Route(s) of administration: Epilesional use; Waiver Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of haemorrhage resulting from a surgical procedure Treatment of cerebrospinal fluid leakage resulting from a neurosurgical procedure

2.2 Indication(s) targeted by the PIP:

Supportive treatment in surgery, for improvement of haemostasis where standard surgical techniques are ineffective and impractical Supportive treatment in surgery, cerebrospinal leakage resulting from neurosurgical procedure

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

All subsets of the paediatric population 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)

2.4 Pharmaceutical Form(s):

Solution for sealant; Sealant matrix

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Study 1 Deleted in adopted UK-PIP (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 the 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 adopted UK-PIP (EMEA-001149-PIP01-11-M05) Study 4 (EVICEL paediatric bleeding study) Open label randomized 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.
Extrapolation, Modeling & Simulation Studies	0	Not applicable
Other Studies	0	Not applicable
Other Measures	0	Not applicable

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	31/07/2022
Deferral of one or more studies contained in the paediatric investigation plan:	Yes