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 change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-100370-PIP01-21-M01

Scope of the Application

Active Substance(s)

EX VIVO EXPANDED AUTOLOGOUS HUMAN CORNEAL EPITHELIAL CELLS CONTAINING STEM CELLS

Condition(s)

Treatment of limbal stem cell deficiency due to ocular burns

Pharmaceutical Form(s)

Living tissue equivalent

Route(s) of Administration

Ophthalmic use

Name / Corporate name of the PIP applicant

Holostem Terapie Avanzate s.r.l.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Holostem Terapie Avanzate s.r.l. submitted to the licensing authority on 23/11/2021 07:45 GMT an application for a Modification

The procedure started on 20/06/2022 10:38 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 change(s) 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-100370-PIP01-21-M01

Of 01/07/2022 12:01 BST

On the adopted decision for EX VIVO EXPANDED AUTOLOGOUS HUMAN CORNEAL EPITHELIAL CELLS CONTAINING STEM CELLS (MHRA-100370-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 EX VIVO EXPANDED AUTOLOGOUS HUMAN CORNEAL EPITHELIAL CELLS CONTAINING STEM CELLS, Living tissue equivalent , Ophthalmic use .

This decision is addressed to Holostem Terapie Avanzate s.r.l., via Glauco Gottardi 100, Modena, Italy, 41125

ANNEX I

1. Waiver

1.1 Condition:

Treatment of limbal stem cell deficiency due to ocular burns The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Living tissue equivalent Route(s) of administration: Ophthalmic use Reason for granting waiver: on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s)

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of limbal stem cell deficiency due to ocular burns

2.2 Indication(s) targeted by the PIP:

Treatment of limbal stem cell deficiency due to ocular burns

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

The paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Living tissue equivalent

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable
Non-Clinical Studies	0	Not applicable
Clinical Studies	1	Study 1 (HLSTM03, HOLOCORE) Multinational, open-label, uncontrolled clinical trial to confirm the activity and safety of autologous corneal limbal stem cell product.
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:	Yes
Date of completion of the paediatric investigation plan:	31/03/2022
Deferral of one or more studies contained in the paediatric investigation plan:	Yes