EMA/68410/2022

# European Medicines Agency decision

P/0066/2022

of 11 March 2022

on the acceptance of a modification of an agreed paediatric investigation plan for ex vivo expanded autologous human corneal epithelium cells containing stem cells (Holoclar), (EMEA-001082-PIP02-11-M03) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0199/2012 issued on 24 August 2012, the decision P/0248/2015 issued on 30 October 2015 and the decision P/0370/2018 issued on 7 December 2018,

Having regard to the application submitted by Holostem Terapie Avanzate S.r.l. on 18 October 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 21 January 2022, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

***Article 1***

Changes to the agreed paediatric investigation plan for ex vivo expanded autologous human corneal epithelium cells containing stem cells (Holoclar), living tissue equivalent, ophthalmic 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 Holostem Terapie Avanzate S.r.l., 100 Via Glauco Gottardi, 41125 – Modena, Italy.

EMA/PDCO/604173/2021
Amsterdam, 21 January 2022

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

EMEA-001082-PIP02-11-M03

## Scope of the application

**Active substance(s):**

Ex vivo expanded autologous human corneal epithelium cells containing stem cells

**Invented name:**

Holoclar

**Condition(s):**

Treatment of limbal stem cell deficiency due to ocular burns

**Authorised indication(s):**

See Annex II

**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.

**Information about the authorised medicinal product:**

See Annex II

## Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Holostem Terapie Avanzate S.r.l. submitted to the European Medicines Agency on 18 October 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/0199/2012 issued on 24 August 2012, the decision P/0248/2015 issued on 30 October 2015 and the decision P/0370/2018 issued on 7 December 2018.

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

The procedure started on 22 November 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)

# Waiver

## *1.1. Condition: treatment of limbal stem cell deficiency due to ocular burns*

The waiver applies to:

- all subsets of the paediatric population from birth to less than 2 years of age;
- living tissue equivalent, ophthalmic use;
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

# 2. Paediatric Investigation Plan

## *2.1. Condition: treatment of limbal stem cell deficiency due to ocular burns*

### 2.1.1. Indication(s) targeted by the PIP

Treatment of limbal stem cell deficiency due to ocular burns

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

From 2 years to less than 18 years of age

### 2.1.3. Pharmaceutical form(s)

Living tissue equivalent

### 2.1.4. Measures

| **Area** | **Number of studies** | **Description** |
|---|---|---|
| Quality-related studies | 0 | Not applicable |
| Non-clinical studies | 0 | Not applicable |
| Clinical studies | 1 | **Study 1**<br>Multicentre, open-label, uncontrolled clinical trial to confirm activity and safety of autologous corneal limbal stem cell product. (**HLSTM03, HOLOCORE)** |
| Extrapolation, modelling and simulation studies | 0 | Not applicable |
| Other studies | 0 | Not applicable |
| Other measures | 0 | Not applicable |

## 3. Follow-up, completion and deferral of PIP

| | |
|---|---|
| Concerns on potential long term safety issues in relation to paediatric use: | Yes |
| Date of completion of the paediatric investigation plan: | By March 2022 |
| 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):

1. Treatment of limbal stem cell deficiency

Authorised indication(s):

- Treatment of adult patients with moderate to severe limbal stem cell deficiency (defined by the presence of superficial corneal neovascularisation in at least two corneal quadrants, with central corneal involvement, and severely impaired visual acuity), unilateral or bilateral, due to physical or chemical ocular burns. A minimum of 1 - 2 mm2 of undamaged limbus is required for biopsy.

# Authorised pharmaceutical form(s):

Living tissue equivalent

# Authorised route(s) of administration:

Implantation