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EPAR summary for the public

Holoclar

ex vivo expanded autologous human corneal epithelial cells containing stem cells

This is a summary of the European public assessment report (EPAR) for Holoclar. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Holoclar.

For practical information about using Holoclar, patients should read the package leaflet or contact their doctor or pharmacist.

What is Holoclar and what is it used for?

Holoclar is a stem-cell treatment used in the eye to replace damaged cells on surface (epithelium) of the cornea, the transparent layer in front of the eye covering the iris (the coloured part).

It is used in adult patients with moderate to severe limbal stem-cell deficiency caused by burns, including chemical burns, to the eyes. Patients with this condition do not have enough limbal stem cells which normally act as a regeneration system, replenishing the outer corneal cells when they get damaged and when they age.

Holoclar is a type of advanced therapy product called a 'tissue engineered product'. It consists of cells taken from the patient's limbus (at the edge of the cornea) and then grown in a laboratory so that they can be used to repair the damaged corneal surface.

Because the number of patients with limbal stem-cell deficiency due to burns to the eyes is low, the disease is considered 'rare', and Holoclar was designated an 'orphan medicine' (a medicine used in rare diseases) on 7 November 2008.

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How is Holoclar used?

Holoclar must only be used by an appropriately trained and qualified eye surgeon in a hospital, and must only be given to the patient whose limbal cells were used to manufacture the medicine.

In the first stage of treatment, a small part of healthy limbal tissue (1–2 mm^2 in size) is taken from the patient in hospital and sent to the manufacturer on the same day. Next, the cells in the tissue are grown in a laboratory and frozen until the date of surgery is confirmed. Thawed cells are used to make Holoclar by growing them on a membrane made of a protein called fibrin. Holoclar, comprising the cells and the membrane, is then sent back to the hospital, where it is immediately surgically implanted in the patient's eye.

Antibiotics to prevent eye infection should be given to patients after limbal tissue has been taken from them. Following the surgery, the patient should receive antibiotics and an appropriate anti-inflammatory medicine.

Holoclar is intended for a single treatment, although treatment can be repeated if the doctor considers it necessary. For further information, see the summary of product characteristics (also part of the EPAR).

How does Holoclar work?

The active substance in Holoclar is the patient's own limbal cells, which include cells from the surface of the cornea and limbal stem cells grown in a laboratory. Before Holoclar is used, the damaged corneal surface tissue of the affected eye is removed. Once implanted in the eye, the corneal cells of Holoclar help to replace the corneal surface, while the limbal stem cells serve as a reservoir of new cells that continuously replenish the cornea.

What benefits of Holoclar have been shown in studies?

Holoclar was shown to be effective in restoring a stable corneal surface in patients with moderate or severe limbal stem-cell deficiency caused by burns in a retrospective study using patients' past medical records. One year after Holoclar implantation, 75 out of 104 patients studied (72%) were judged to have had successful implants based on the presence of stable corneal surface with no surface defects and little or no ingrown blood vessels (a common feature of limbal stem-cell deficiency). There were also reductions in patients' symptoms, such as pain and inflammation, and improvements in vision.

What are the risks associated with Holoclar?

The most common side effect with Holoclar (seen in more than 1 patient in 10) is blepharitis (inflammation of the eye lid). For the full list of all side effects and restrictions, see the package leaflet.

Why is Holoclar approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that Holoclar treatment was effective in restoring healthy corneal surfaces in patients with moderate or severe limbal stem-cell deficiency caused by burns as well as in improving their symptoms and vision. The Committee noted that that moderate to severe forms of limbal stem-cell deficiency are serious conditions which, if untreated, can lead to severe reduction or complete loss of vision. As the side effects of Holoclar treatment are generally manageable, the CHMP concluded that Holoclar's benefits outweigh its risks and recommended that it be approved for use in the EU.

The conclusion on the benefit-risk balance of Holoclar is based on results of two retrospective studies (using past medical records), and the company is to provide further data from a prospective study (that records outcomes during the course of the study).

Holoclar has therefore been given 'conditional approval'. This means that there is more evidence to come about the medicine, which the company is required to provide. Every year, the European Medicines Agency will review any new information that becomes available and this summary will be updated as necessary.

What information is still awaited for Holoclar?

Since Holoclar has been granted a conditional approval, the company that markets Holoclar will provide further data on Holoclar. The company is to provide data on the benefits and risks of Holoclar from a prospective clinical study.

What measures are being taken to ensure the safe and effective use of Holoclar?

A risk management plan has been developed to ensure that Holoclar is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Holoclar, including the appropriate precautions to be followed by healthcare professionals and patients.

In addition, the company that makes Holoclar will provide healthcare professionals with educational material on the safe use of this treatment, including on the selection and follow-up of patients and on reporting side effects. Educational material will also be provided to patients undergoing treatment.

Further information can be found in the summary of the risk management plan.

Other information about Holoclar

The European Commission granted a marketing authorisation valid throughout the European Union for Holoclar on 17 February 2015.

The full EPAR and risk management plan summary for Holoclar can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Holoclar, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

The summary of the opinion of the Committee for Orphan Medicinal Products for Holoclar can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

This summary was last updated in 02-2015.