NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ex vivo expanded autologous human corneal epithelial cells for treating moderate to severe limbal stem cell deficiency due to ocular burns

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ex vivo expanded autologous human corneal epithelial cells containing stem cells within its marketing authorisation for treating moderate to severe limbal stem cell deficiency due to ocular burns.

Background

The cornea is the clear, rigid layer covering the front of the eye and it is divided in 4 quadrants: superior, temporal, inferior and nasal. Cells on the cornea surface are constantly being renewed and replaced by limbal stem cells which are located in the ocular surface between the cornea and the bulbar conjunctiva. An injury to the source of the limbal stem cells can cause a deficiency of these cells known as limbal stem deficiency (LSCD), reducing the renewal and replacement of the surface of the cornea. This results in the cornea being repaired by different types of eye cell and excessive ingrowth of blood vessels (neovascularisation), which can make the cornea opaque and impair vision. Ocular burns because of chemicals or heat can damage these stem cells. Moderate to severe LSCD is defined by the presence of superficial corneal neovascularisation in at least 2 corneal quadrants, with central corneal involvement, and severely impaired visual acuity.

The estimated prevalence of LSCD due to ocular burns in Europe is 0.3 in 10,000 people[1], which is equivalent to about 1800 people in England. The number of corneal transplants for ocular surface burns is thought to be very small. It is estimated that approximately 90 to 100 people in England would be eligible for treatment with ex vivo expanded autologous human corneal epithelial cells containing stem cells[2].

The aim of current treatment is to restore a healthy conjunctival and corneal surface. Treatments include topical steroids, ocular lubricants, bandage contact lenses, autologous serum eye drops, oral and/or topical vitamin C and oral tetracycline. Historically, LSCD has been treated with surgical procedures based on tissue therapy. Tissue from the healthy eye has been used for conjunctival limbal autografts for people with unilateral LSCD, and tissue from a cadaver or a relative donor has been used for limbal epithelial stem cells allografts for bilateral disease. However these procedures are associated with a high risk of allograft rejection and damage to the healthy eye. There are no

specific treatments available for treating LSCD due to physical or chemical ocular burns.

The technology

Ex vivo expanded autologous human corneal epithelial cells containing stem cells (Holoclar, Chiesi Farmaceutici) is a treatment used in the eye to replace damaged cells on corneal surface. It consists of cells taken from the patient's limbus (at the edge of the cornea) and then grown in a laboratory and frozen until the date of surgery is confirmed. The cells are grown on a membrane made of a protein called fibrin and the final product is then sent back to the hospital, where it is immediately surgically implanted in the patient's eye.

Ex vivo expanded autologous human corneal epithelial cells containing stem cells has a conditional marketing authorisation in the UK for moderate to severe limbal stem cell deficiency (defined by the presence of superficial corneal neovascularisation in at least 2 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 mm^2 of undamaged limbus is required for biopsy. As part of the conditional marketing authorisation the company is conducting a prospective, open-label, uncontrolled interventional study to assess the efficacy and safety of autologous cultivated limbal stem cells grafting for restoration of corneal epithelium in patients with limbal stem cell deficiency due to ocular burns.

Intervention(s)	Ex vivo expanded autologous human corneal epithelial cells containing stem cells
Population(s)	Adults with moderate to severe limbal stem cell deficiency (defined by th+e presence of superficial corneal neovascularisation in at least 2 corneal quadrants, with central corneal involvement, and severely impaired visual acuity), unilateral or bilateral, due to physical or chemical ocular burns and a minimum of 1 - 2 mm^2 of undamaged limbus
Comparators	For people with unilateral limbal stem cell deficiency: • conjunctival limbal autograft • best supportive care For people with bilateral limbal stem cell deficiency: • conjunctival limbal autograft • limbal epithelial stem cells allografts • best supportive care

Outcomes	The outcome measures to be considered include: • clinical parameters of limbal stem cell deficiency including stability and transparency of the corneal epithelium and superficial corneal neovascularisation • symptoms of limbal stem cell deficiency including pain, burning and photophobia • visual acuity (the affected eye) • visual acuity (the whole person) • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. The costs and effects of best supportive care when given in combination with the intervention should be taken into account. Best supportive care includes topical steroids, ocular lubricants, bandage contact lenses, autologous serum eye drops, oral and/or topical vitamin C and oral tetracycline.
Related NICE recommendations and NICE Pathways	Related Interventional Procedures: 'Corneal endothelial transplantation' (2009) NICE interventional procedures guidance 304 'Tissue-cultured limbal stem cell allograft transplantation for regrowth of corneal epithelium' (2007) NICE

	interventional procedures guidance 216 Related NICE Pathways: Eye conditions (2015) NICE pathway. http://pathways.nice.org.uk/pathways/eye-conditions
Related National Policy	Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 3, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf NHS England (2014) Manual for prescribed specialised services 2013/14. Chapter 12. D12 - Adult specialist opthalmology services. NHS England (2013) NHS standard contract for specialised ophthalmology (adult). Schedule 2 - the services - A. the specifications. NHS England (2013) 2013/14 NHS standard contract for osteo-odonto-keratoprosthesis service for corneal blindness (adults). particulars, schedule 2- the services, a- service specification

References

1. European Medicines Agency (2015) Public summary of opinion on orphan designation. Accessed July 2015.

2. Company communication.