European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of *ex vivo* expanded autologous human corneal epithelium containing stem cells for the treatment of corneal lesions, with associated corneal (limbal) stem cell deficiency, due to ocular burns

On 7 November 2008, orphan designation (EU/3/08/579) was granted by the European Commission to Chiesi Farmaceutici S.P.A., Italy, for *ex vivo* expanded autologous human corneal epithelium containing stem cells for the treatment of corneal lesions, with associated corneal (limbal) stem cell deficiency, due to ocular burns.

What are corneal lesions, with associated corneal (limbal) stem cell deficiency, due to ocular burns?
Corneal lesions are areas of damage to the cornea, the transparent surface at the front of the eye in front of the pupil. The surface of the cornea is constantly being renewed and replaced by the production of new cells that are produced by 'stem cells' in the lower layers of the cornea, called the 'basal limbal epithelium'. Ocular burns (burns to the eye) because of chemicals or heat can damage these stem cells. This can cause a deficiency (low number) of the stem cells, reducing the renewal and replacement of the surface of the cornea. This results in the cornea being repaired by different types of eye cell, which can make the cornea opaque and impair the patient's vision.
This condition is considered to be debilitating because of loss of vision.

What treatments are available?
There are no authorised products for this condition in the Community, although surgery, such as transplanting a cornea from a donor who has recently died, can been used. Although this can restore the patient's vision, failure of the cornea can occur at any time after the transplant.
Ex vivo expanded autologous human corneal epithelium containing stem cells could be of potential significant benefit for the treatment of corneal lesions, with associated corneal (limbal) stem cell deficiency, due to ocular burns, because they might act differently from other methods. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

What is the estimated number of patients affected by the condition?
At the time of designation corneal lesions, with associated corneal (limbal) stem cell deficiency, due to ocular burns affected approximately 0.3 in 10,000 people in the European Union (EU)[*]. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around 151,000 people.

[*] Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 27), Norway, Iceland and Liechtenstein. This represents a population of 502,282,000 (Eurostat 2008).

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How is this medicine expected to work?
This product is made of a small sample of cells that are taken from an undamaged part of the basal limbal epithelium in the patient's cornea. The cells are attached to a 'glue' made of chemically-modified fibrin and grown in the laboratory to produce a replacement surface (epithelium) for the cornea. The epithelium is then implanted into the patient's damaged eye or eyes. The stem cells contained within the epithelium then help the cornea to regenerate, restoring the patient's vision.

What is the stage of development of this medicine?
The effects of this product have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with corneal lesions, with associated corneal (limbal) stem cell deficiency, due to ocular burns were ongoing.

At the time of submission, this product was not authorised anywhere worldwide for this condition or designated as orphan medicinal product elsewhere for this condition at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted a positive opinion on 10 September 2008 recommending the granting of this designation.

Opinions on orphan medicinal product designations are based on the following three criteria:
- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the Community) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

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Translations of the active ingredient and indication in all EU languages and Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Ex-vivo expanded autologous human corneal epithelium containing stem cells	Treatment of corneal lesions, with associated corneal (limbal) stem cell deficiency, due to ocular burns
Bulgarian	Разширен ex-vivo автоложен човешки роговичен епител, съдържащ стволови клетки	Лечение на роговични лезии, съпътствани от недостиг на роговични (лимбални) стволови клетки, вследствие на изгаряния на окото
Czech	Autologní lidský rohovkový epitel expandovaný ex-vivo	Léčba lezí rohovky způsobených popálením spojená s deficitem korneálních (limbálních) kmenových buněk
Danish	Ex vivo-ekspanderet autologt humant corneaepitel indeholdende stamceller	Behandling af cornealæsioner med associeret corneal (limbal) stamcelledeficiens, forårsaget af forbrænding af øjet
Dutch	Ex-vivo geëxpandeerd autoloog humaan corneaal epitheel dat stamcellen bevat	Behandeling van corneale laesies, met daarmee samenhangende corneale (limbale) stamceldeficiëntie, als gevolg van oculaire brandwonden
Estonian	Ex vivo kasvatatud autoloogne tüvirakke sisaldav inimese sarvkesta epiteel	Silma põletustest tingitud sarvkestakahjustuste, ravi, mis on seotud . sarvkesta (limbaalsete) tüvirakkude puudulikkusega
Finnish	Ex vivo kasvatettu autologinen, kantasoluja sisältävä, ihmisen sarveiskalvon epiteeli	Silmän palovammoista johtuvien sarveiskalvovaurioiden hoito, joihin liittyy sarveiskalvon (limbaalisten) kantasolujen puute
French	Épithélium cornéen humain autologue contenant des cellules souches et cultivé ex-vivo	Traitement des lésions cornéennes, associées à un déficit en cellules souches cornéennes (limbiques), dues à des brûlures oculaires
German	Ex vivo vermehrtes autologes menschliches Corneaepithel, welches Stammzellen enthält	Behandlung von Cornealäsionen, hervorgerufen durch Augenverätzungen, verbunden mit einem Mangel an cornealen (limbalen) Stammzellen
Greek	Ex-vivo διογκούμενο αυτόλογο ανθρώπινο επιθήλιο κερατοειδούς περιέχον βλαστοκύτταρα	Θεραπεία αλλοιώσεων του κερατοειδούς, με σχετιζόμενη έλλειψη βλαστοκυττάρων κερατοειδούς (σκληροκερατοειδής ζώνη), που οφείλονται σε οφθαλμικά εγκαύματα
Hungarian	Ex.vivo kifejlesztett autológ humán szaruhártya hámszövet, amely őssejtet tartalmaz	A szem égési sérülésének következtében kialakult, szaruhártya- (limbális) sejthiánnyal társuló szaruhártya sérülés kezelésére
Italian	Epitelio corneale umano autologo, espanso ex-vivo e contenente cellule staminali	Trattamento di lesioni corneali, con deficit di cellule staminali corneali (limbali), dovuto a ustioni oculari
Latvian	Cilmes šūnu saturošas, ex-vivo audzētas autologas cilvēka radzenes epitēlija šūnas	Apdegumu izraisītu radzenes bojājumu ārstēšana, kas saistīti ar radzenes (radzenes robežšūnu) cilmes šūnu trūkumu
Lithuanian	Ex-vivo išvystytas autologinis žmogaus ragenos epitelis, turintis kamieninių ląstelių	Ragenos pažeidimų, susijusių su ragenos krašto (limbus cornea) kamieninių ląstelių trūkumu esant akies nudegimams, gydymas

Maltese	Epitelju awtologu uman tal-kornea mkabbar ex-vivo, li fih ċelluli staminali	Kura ta' leżjonijiet fil-korneja assoċjati ma' nuqqas ta' ċelluli staminali (limbali) tal-kornea, ikkawżati minn ħruq fl-għajn
Polish	Hodowany ex-vivo autologiczny ludzki nabłonek rogówki zawierający komórki macierzyste	Leczenie uszkodzeń rogówki, z towarzyszącym niedoborem komórek macierzystych rogówki (rąbka), spowodowanych oparzeniami oczu
Portuguese	Epitélio da córnea humana autólogo expandido ex vivo contendo células estaminais	Tratamento de lesões da córnea associadas a com deficiência associada de células estaminais córneo-limbais, devido a queimaduras oculares
Romanian	Epiteliu corneean uman autolog, dezvoltat ex-vivo care conține celule stem	Tratamentul leziunilor corneene asociate cu deficitde celule stem corneene, determinate de arsuri oculare
Slovak	Ex-vivo expandovaný autológový ľudský rohovkový epitel obsahujúci kmeňové bunky	Liečba rohovkových lézií, spojených s nedostatkom rohovkových (limbálnych) kmeňových buniek, v dôsledku popálenín oka.
Slovenian	Ex vivo ekspandiran avtologen človeški roženični epitelij, ki vsebuje matične celice	Zdravljenje roženičnih lezij, ki so posledica opeklin očesa, in so povezane s pomanjkanjem roženičnih (limbusnih) matičnih celic
Spanish	Epitelio corneal humano autólogo expandido ex-vivo que contiene células madre	Tratamiento de lesiones corneales, con deficiencia de células madre corneales (limbo esclerocorneal), debidas a quemaduras oculares
Swedish	Ex-vivo-expanderat autologt humant korneaepitel innehållande stamceller	Behandling av kornealesioner med åtföljande brist på korneala (limbala) stamceller, till följd av bränskador på ögat
Norwegian	Ex vivo-ekspandert autologt human korneal epitel med stamceller	Behandling av kornealesjoner assosiert med korneal (limbal) stamcellemangel på grunn av okulære brannskader
Icelandic	Samgena þekjuvefur, sem hefur verið látinn vaxa utan líkamans, úr mannaglæru með stofnfrumum	Meðferð við vefskemmdum í glæru, með samfara skorti á glærustofnfrumum, vegna efnabruna í augum