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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Ex-vivo-expanded autologous human keratinocytes containing epidermal stem cells transduced with a *LAMB3*-encoding retroviral vector for the treatment of epidermolysis bullosa

On 19 March 2015, orphan designation (EU/3/15/1465) was granted by the European Commission to Chiesi Farmaceutici S.p.A., Italy, for ex-vivo-expanded autologous human keratinocytes containing epidermal stem cells transduced with a *LAMB3*-encoding retroviral vector for the treatment of epidermolysis bullosa.

What is epidermolysis bullosa?

Epidermolysis bullosa describes a group of inherited diseases of the skin, in which the skin is very fragile and forms severe blisters upon minor mechanical friction or injury. In most cases, symptoms of epidermolysis bullosa appear from birth, although for some forms symptoms may not occur until adulthood. The diseases are caused by mutations (changes) in the genes responsible for the production of certain proteins that make the skin strong and elastic, such as collagen or keratins.

Epidermolysis bullosa is a long-term debilitating and life-threatening condition because the severe blistering and associated scarring and deformities result in poor quality of life and may also reduce life expectancy.

What is the estimated number of patients affected by the condition?

At the time of designation, epidermolysis bullosa affected approximately 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 31,000 people[*], and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

[*]Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 512,900,000 (Eurostat 2015).

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What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU to treat epidermolysis bullosa. A high standard of personal hygiene and skincare were recommended to help blisters heal, to avoid infections and to protect the skin from damage. Painkillers were also used. Surgery was sometimes necessary if there were complications such as deformed hands or the development of skin cancer.

How is this medicine expected to work?

One of the genes whose mutation can cause epidermolysis bullosa is known as *LAMB3*, which is needed for normal production of a protein called laminin-332 that helps to hold skin layers together.

This medicine is a skin graft prepared individually for patients who have epidermolysis bullosa due to the *LAMB3* mutation. It consists of a layer of the patient's own skin cells, including the stem cells needed to grow new skin. These cells are grown outside the body and modified with a virus that has been engineered to carry a normal copy of the *LAMB3* gene into the cells. The cells are then returned to the patient as a skin graft over areas of blistered skin, where they are expected to produce skin cells with normal laminin-332, correcting the cause of the condition and preventing blister formation.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with epidermolysis bullosa were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for epidermolysis bullosa or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 February 2015 recommending the granting of this designation.

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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 EU) 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.

For more information

Sponsor's contact details:

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For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Ex-vivo-expanded autologous human keratinocytes containing epidermal stem cells transduced with a *LAMB3*-encoding retroviral vector	Treatment of epidermolysis bullosa
Bulgarian	Ex vivo експандирани автоложни човешки кератиноцити, съдържащи епидермални стволови клетки, трансдуцирани с *LAMB3*-кодиращ ретровирусен вектор	Лечение на булозна епидермолиза
Croatian	Ex vivo umnoženi autologni ljudski keratinociti koji sadrže epidermalne matične stanice transducirane retrovirusnim vektorom koji kodira za *LAMB3*	Liječenje bulozne epidermolize
Czech	Ex vivo expandované autologní lidské keratinocyty obsahující epidermální kmenové buňky transdukované retrovirovým vektorem kódujícím gen *LAMB3*	Léčba bulózní epidermolýzy
Danish	Ex vivo ekspanderede autologe humane keratinocytter, der indeholder epidermale stamceller transduceret med en *LAMB3*-indkodende retroviral vektor	Behandling af epidermolysis bullosa
Dutch	Ex-vivo geëxpandeerde autologe humane keratinocyten die epidermale stamcellen bevatten die zijn getransduceerd met een retrovirale vector die codeert voor *LAMB3*	Behandeling van epidermolysis bullosa
Estonian	*LAMB3*-kodeeriva retroviirusvektoriga transdutseeritud epidermise tüvirakke sisaldavad *ex vivo* kasvatatud autoloogsed inimese keratinotsüüdid	Bulloosse epidermolüüsi ravi
Finnish	Ex vivo monistetut autologiset ihmisen keratinosyytit, joiden mukana on epidermaalisia kantasoluja, joihin on siirretty *LAMB3*-geeniä koodaava retroviraalinen vektori	Epidermolysis bullosan hoito
French	Kératinocytes humains autologues amplifiés *ex vivo* contenant des cellules souches épidermiques transduites avec un vecteur rétroviral codant pour le *LAMB3*	Traitement de l'épidermolyse bulleuse
German	Autologe ex vivo expandierte menschliche Keratinozyten, die mit einem *LAMB3* kodierenden retroviralen Vektor transduzierte epidermale Stammzellen enthalten	Behandlung der Epidermolysis bullosa

[1] At the time of designation

Language	Active ingredient	Indication
Greek	Ex vivo πολλαπλασιασμένα αυτόλογα ανθρώπινα κερατινοκύτταρα που περιέχουν επιδερμικά βλαστικά κύτταρα επωασμένα με ρετροϊκό φορέα ο οποίος κωδικοποιεί το *LAMB3*	Θεραπεία της πομφολυγώδους επιδερμόλυσης
Hungarian	*LAMB3* gént kódoló retroviralis vektorral átalakított epidermalis őssejteket tartalmazó, ex vivo kiterjesztett autológ humán keratinociták	Epidermolysis bullosa kezelése
Italian	Cheratinociti umani autologhi espansi *ex vivo* contenenti cellule staminali epidermiche trasdotte con un vettore retrovirale codificante per il gene *LAMB3*	Trattamento della epidermolisi bollosa
Latvian	*Ex vivo* pavairoti autologi cilvēka keratinocīti, kas satur epidermas cilmes šūnas, kas transducētas ar *LAMB3*-kodējošu retrovīrusa vektoru	Bulozās epidermolīzes ārstēšanai
Lithuanian	*Ex vivo* padauginti autologiniai žmogaus keratinocitai, kuriuose yra epidermio kamieninių ląstelių, transdukuotų su *LAMB3* koduojančiu retrovirusiniu vektoriumi	Pūslinės epidermolizės gydymas
Maltese	Keratinoċiti awtologi umani imkabbra ex vivo li fihom ċelluli staminali tal-epidermide trasformati permezz ta' vettur retrovirali li jikkodifika *LAMB3*	Kura tal-epidermolisi bullosa
Polish	Namnożone ex vivo autologiczne ludzkie keratynocyty zawierające komórki macierzyste naskórka po transdukcji wektorem retrowirusowym kodującym *LAMB3*	Pęcherzowe oddzielanie się naskórka
Portuguese	Queratinócitos humanos autólogos expandidos ex vivo contendo células estaminais epidérmicas transduzidas com um vector retroviral codificador do *LAMB3*	Tratamento da epidermólise bulhosa
Romanian	Keratinocite umane autologe expandate ex vivo conţinând celule stem epidermale transduse cu un vector retroviral codant pentru *LAMB3*	Tratamentul epidermolizei buloase
Slovak	Ex vivo kultivované autológne ľudské keratinocyty obsahujúce epidermálne kmeňové bunky transdukované pomocou retrovirálneho vektora kódujúceho *LAMB3*	Liečba epidermolysis bullosa
Slovenian	Ex vivo ekspandirani avtologni keratinociti, ki vsebujejo epidermalne matične celice, transducirane z retrovirusnim vektorjem, ki kodira *LAMB3*	Zdravljenje bulozne epidrmolize
Spanish	Queratinocitos autólogos humanos expandidos *ex vivo* que contienen células madre epidérmicas transducidas con un vector retroviral codificador de *LAMB3*	Tratamiento de la epidermolisis bullosa

Language	Active ingredient	Indication
Swedish	Ex vivo-expanderade autologa humana keratinocyter som innehåller epidermala stamceller transducerade med en *LAMB3*-kodande retroviral vektor	Behandling av epidermolysis bullosa
Norwegian	Ex vivo ekspanderte autologe humane keratinocytter som inneholder epidermale stamceller transdusert med en *LAMB3*-kodende retrovirusvektor	Behandling av epidermolysis bullosa
Icelandic	Ex vivo útvíkkaðar samgena hyrnisfrumur manna sem innihalda húðþekjustofnfrumur sem eru veiruleiddar með *LAMB3*-kóðandi retróveiruferju	Meðferð á epidermolysis bullosa