27 March 2017
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Public summary of opinion on orphan designation

Ex-vivo-expanded autologous keratinocytes transduced with retroviral vector containing the *COL7A1* gene for the treatment of epidermolysis bullosa

On 27 February 2017, orphan designation (EU/3/17/1835) was granted by the European Commission to Ser-mes Planificación SL, Spain, for ex-vivo-expanded autologous keratinocytes transduced with retroviral vector containing the COL7A1 gene (also known as EB-101) for the treatment of epidermolysis bullosa.

What is epidermolysis bullosa?

Epidermolysis bullosa is a group of inherited diseases of the skin, in which the skin is very fragile and forms severe blisters after even minor friction (rubbing) or injury. In most cases, symptoms of epidermolysis bullosa appear from birth, but 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).

What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU to treat epidermolysis bullosa. Good personal hygiene and skincare were recommended to help blisters heal, to avoid

[*]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 515,700,000 (Eurostat 2017).

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infections and to protect the skin from damage. Painkillers were also used. Surgery was sometimes necessary for complications such as deformed hands or the development of skin cancer.

How is this medicine expected to work?

This medicine is prepared individually for patients who have epidermolysis bullosa due to mutations in the *COL7A1* gene. This gene normally produces a substance called collagen 7 that helps hold skin layers together. The medicine consists of patient's own skin cells called keratinocytes, which are modified in the laboratory with a virus that has been engineered to transfer the normal *COL7A1* gene into the cells. The modified cells are grown in a layer to make a skin graft that can be surgically transplanted back to the patient. The modified skin cells are then expected to grow normally and produce collagen 7, correcting the cause of the condition, improving blister healing 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 this medicine in patients with epidermolysis bullosa were ongoing.

At the time of submission, the 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 19 January 2017 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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 keratinocytes transduced with retroviral vector containing the *COL7A1* gene	Treatment of epidermolysis bullosa
Bulgarian	Ex vivo експандирани автоложни кератиноцити, трансдуцирани с ретровирусен вектор, съдържащ *COL7A1* ген	Лечение на булозна епидермолиза
Croatian	Ex vivo prošireni autologni keratinociti transducirani retroviralnim vektorom koji sadrži *COL7A1* gen	Liječenje bulozne epidermolize
Czech	Autologní keratinocyty expandované ex-vivo transdukované retrovirálním vektorem obsahující gen *COL7A1*	Léčba bulózní epidermolýzy
Danish	Ex-vivo-ekspanderede autologe keratinocytter transduceret med retroviral vektor, der indeholder *COL7A1*-genet	Behandling af epidermolysis bullosa
Dutch	Ex vivo geëxpandeerde autologe keratinocyten getransduceerd met retrovirale vector die het *COL7A1*-gen bevat	Behandeling van epidermolysis bullosa
Estonian	*COL7A1* geeni sisaldava retroviirusvektoriga transdutseeritud ex vivo kasvatatud autoloogsed keratinotsüüdid	Bulloosse epidermolüüsi ravi
Finnish	Ex-vivo monistetut autologiset keratinosyytit, joihin on siirretty retrovirusvektori, joka sisältää *COL7A1*-geenin	Epidermolysis bullosan hoito
French	Kératinocytes autologues expansés ex-vivo transduits avec un vecteur rétroviral contenant le gène *COL7A1*	Traitement de l'épidermolyse bulleuse
German	Ex-vivo expandierte autologe Keratinozyten, transduziert mit retroviralem Vektor, der das *COL7A1*-Gen enthält	Behandlung der Epidermolysis bullosa
Greek	Ex vivo πολλαπλασιασμένα αυτόλογα κερατινοκύτταρα επωασμένα με ρετροϊϊκό φορέα ο οποίος περιέχει το γονίδιο *COL7A1*	Θεραπεία της πομφολυγώδους επιδερμόλυσης
Hungarian	Ex-vivo expandált retrovirális vektorral transzdukált autológ keratinociták, melyek tartalmazzák a *COL7A1* gént	Epidermolysis bullosa kezelése
Italian	Cheratinociti autologhi espansi ex vivo trasdotti con un vettore retrovirale contenente il gene *COL7A1*	Trattamento della epidermolisi bollosa
Latvian	*Ex vivo* pavairoti autologi keratinocīti, kas transducēti ar retrovīrusa vektoru, kas satur *COL7A1* gēnu	Bulozās epidermolīzes ārstēšanai
Lithuanian	*Ex vivo* pagausinti autologiniai keratinocitai, transdukuoti su retrovirusiniu vektoriumi, turinčiu *COL7A1* geną	Pūslinės epidermolizės gydymas
Maltese	Keratinoċiti awtologi mkabbra ex-vivo transdotti b'vettur retrovirali li fih il-ġene *COL7A1*	Kura tal-epidermolisi bullosa

[1] At the time of designation

Language	Active ingredient	Indication
Polish	Namnożone ex vivo autologiczne keratynocyty transdukowane wektorem retrowirusowym zawierającym gen *COL7A1*	Pęcherzowe oddzielanie się naskórka
Portuguese	Queratinócitos autólogos expandidos *ex-vivo*, transduzidos com um vetor retroviral contendo o gene *COL7A1*	Tratamento da epidermólise bulhosa
Romanian	Keratinocite autologe expandate ex-vivo transduse cu un vector retroviral ce conține gena *COL7A1*	Tratamentul epidermolizei buloase
Slovak	Ex-vivo-rozšírené autológne keratinocyty transdukované retrovirovým vektorom, ktorý obsahuje gén *COL7A1*	Liečba epidermolysis bullosa
Slovenian	Ex vivo ekspandirani avtologni keratinociti, transducirani z retrovirusnim vektorjem, ki vsebuje gen *COL7A1*	Zdravljenje bulozne epidrmolize
Spanish	Queratinocitos autólogos expandidos ex vivo transducidos con un vector retroviral que contiene el gen *COL17A1*	Tratamiento de la epidermolisis bullosa
Swedish	Ex vivo-expanderade autologa keratinocyter som är transducerade med en retroviral vektor som innehåller *COL7A1*-genen	Behandling av epidermolysis bullosa
Norwegian	Ex-vivo-ekspanderte autologe keratinocytter transdusert med retroviral vektor som inneholder genet *COL7A1*	Behandling av epidermolysis bullosa
Icelandic	Sjálfmyndaðar hyrnisfrumur, auknar ex-vivo, veiruleiddar með retróveiruhamlandi genaferju með *COL7A1* geninu	Meðferð á epidermolysis bullosa