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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous dermal fibroblasts genetically modified ex vivo with a lentiviral vector containing the human *COL7A1* gene for the treatment of epidermolysis bullosa

On 28 April 2016, orphan designation (EU/3/16/1642) was granted by the European Commission to Intrexon Actobiotics, Belgium, for autologous dermal fibroblasts genetically modified ex vivo with a lentiviral vector containing the human *COL7A1* gene (also known as INXN-3002) 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 upon minor mechanical friction 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 0.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 36,000 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 513,700,000 (Eurostat 2016).

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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. Good 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 for complications such as deformed hands or the development of skin cancer.

How is this medicine expected to work?

COL7A1 is a gene that produces collagen 7, which helps to hold skin layers together. Mutations in this gene can cause a type of epidermolysis bullosa called dystrophic epidermolysis bullosa.

This medicine is prepared individually for patients who have epidermolysis bullosa due to the *COL7A1* mutations. It consists of patient's own cells called fibroblasts. These cells are grown in the laboratory and modified with a virus that has been engineered to transfer normal *COL7A1* gene into the cells. The cells are then returned to the patient by an injection into the skin, where they are expected to produce collagen 7, 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, no clinical trials with the medicine in patients with epidermolysis bullosa had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for epidermolysis bullosa. Orphan designation of the medicine had been granted in USA for dystrophic epidermolysis bullosa.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 23 March 2016 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	Autologous dermal fibroblasts genetically modified ex vivo with a lentiviral vector containing the human *COL7A1* gene	Treatment of epidermolysis bullosa
Bulgarian	Автоложни дермални фибробласти генетично модифицирани екс виво с лентивирусен вектор, съдържащ човешкия *COL7A1* ген	Лечение на булозна епидермолиза
Croatian	Autologni kožni fibroblasti genetički modificirani ex vivo sa lentivirusnim vektorom koji sadrži ljudski gen *COL7A1*	Liječenje bulozne epidermolize
Czech	Autologní dermální fibroblasty geneticky modifikovány ex vivo s lentivirovým vektorem obsahující lidský gen *COL7A1*	Léčba bulózní epidermolýzy
Danish	Autologe hudfibroblaster genetisk modificeret ex vivo med en lentiviral vektor, der indeholder det humane *COL7A1*-gen	Behandling af epidermolysis bullosa
Dutch	Autologe dermale fibroblasten genetisch ex vivo gemodificeerd met een lentivirale vector welke het humane *COL7A1* gen bevat	Behandeling van epidermolysis bullosa
Estonian	Autoloogsed naha fibroblastid, mida on geneetiliselt muundatud ex vivo inimese *COL7A1* geeni sisaldava lentiviraalse vektoriga	Bulloosse epidermolüüsi ravi
Finnish	Autologiset ihon fibroblastit, jotka on geneettisesti ex vivo -muokattu yhdessä ihmisen *COL7A1* geenin sisältävän lentivirusvektorin kanssa	Epidermolysis bullosan hoito
French	Fibroblastes dermiques autologues génétiquement modifiés ex vivo avec un vecteur lentiviral contenant le gène humain *COL7A1*	Traitement de l'épidermolyse bulleuse
German	Autologe dermale Fibroblasten, ex vivogentechnisch verändertmit einem lentiviralen Vektor der das humane *COL7A1*-Gen enthält	Behandlung der Epidermolysis bullosa
Greek	Αυτόλογες δερματικες ινοβλάστες γενετικώς τροποποιημένες ex vivo με ένα λεντιϊικό φορέα που περιέχει το ανθρώπινο γονίδιο *COL7A1*	Θεραπεία της πομφολυγώδους επιδερμόλυσης
Hungarian	Humán *COL7A1* gént tartalmazó lentivirális vektorral ex vivo genetikailag módosított autológ dermális fibroblasztok	Epidermolysis bullosa kezelése
Italian	Fibroblasti dermici autologhi geneticamente modificati ex vivo con un vettore lentivirale contenenti il gene umano *COL7A1*	Trattamento della epidermolisi bollosa
Latvian	Autologi ādas fibroblasti, kas ģenētiski modificēti *ex vivo* ar lentivīrusa vektoru, kas satur cilvēka *COL7A1* gēnu	Bulozās epidermolīzes ārstēšanai

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	Genetiškai *ex vivo* modifikuoti autologiniai odos fibroblastai su lentiviruso vektoriumi, turinčiu žmogaus *COL7A1* geną	Pūslinės epidermolizės gydymas
Maltese	Fibroblasti dermali awtologi modifikati ġenetikament ex vivo ma' vettur lentiviral li fih il-ġene ta' *COL7A1*	Kura tal-epidermolisi bullosa
Polish	Autologiczne ludzkie fibroblasty skórne genetycznie zmodyfikowane ex vivo wektorem lentiwirusowym zawierającym gen *COL7A1*	Pęcherzowe oddzielanie się naskórka
Portuguese	Fibroblastos dérmicos autólogos geneticamente modificados ex vivo com um vetor lentiviral contendo o gene humano *COL7A1*	Tratamento da epidermólise bulhosa
Romanian	Fibroblaste dermice autologe modificate genetic *ex vivo* cu un vector lentiviral care conţine gena umană *COL7A1*	Tratamentul epidermolizei buloase
Slovak	Autológne dermálne fibroblasty geneticky modifikované ex vivo s lentivirovým vektorom obsahujúcim ľudský gén *COL7A1*	Liečba epidermolysis bullosa
Slovenian	Avtologni kožni fibroblasti, gensko spremenjeni ex vivo z lentivirusnim vektorjem, ki vsebuje gen gen *COL7A1*	Zdravljenje bulozne epidrmolize
Spanish	Fibroblastos dérmicos autólogos modificados genéticamente ex vivo con un vector lentiviral que contiene el gen humano de *COL7A1*	Tratamiento de la epidermolisis bullosa
Swedish	Autologa dermala fibroblaster genetiskt modifierade ex vivo med en lentivirusvektor innehållande human *COL7A1* gen	Behandling av epidermolysis bullosa
Norwegian	Autologe dermale fibroblaster genetisk modifisert ex vivo med en lentiviral vektor som inneholder det humane *COL7A1*-genet	Behandling av epidermolysis bullosa
Icelandic	Samgena skinn trefjakímfrumur breytt erfðafræðilega *ex vivo* með lentiviral vektor sem kóðar fyrir manna *COL7A1* geni	Meðferð á epidermolysis bullosa