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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Bilayer engineered skin composed of keratinocytes from the patient (autologous) and fibroblasts from a donor (allogeneic) embedded in a plasma matrix for the treatment of epidermolysis bullosa

First publication	13 May 2009
Rev.1: change of name	7 June 2013
Rev.2: transfer of sponsorship	4 March 2015

Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 22 May 2006, orphan designation (EU/3/06/369) was granted by the European Commission to Cellerix S.L., Spain, for bilayer engineered skin composed of keratinocytes from the patient (autologous) and fibroblasts from a donor (allogeneic) embedded in a plasma matrix for the treatment of epidermolysis bullosa.

The sponsor changed name to Cellerix S.A. in September 2008 and then to TiGenix S.A.U. in February 2013.

The sponsorship was transferred to Biodan Yelah S.L., Spain, in December 2014.

What is epidermolysis bullosa?

Epidermolysis bullosa describes a group of diseases of the skin and mucous membranes. Patients with epidermolysis bullosa have extremely fragile skin and recurrent blister formation, resulting from minor mechanical friction or injury. Epidermolysis bullosa is caused by defective production of collagen. Collagen is the core substance that makes up the matrix that surrounds cells (extracellular matrix) in the body. It is essential for the support of tissues and gives cells structure from the outside. There are several types of collagen, each with unique function. Epidermolysis bullosa patients have a change in their genetic material (the gene coding for collagen VII has a mutation) and cannot produce collagen VII, a type of collagen essential for the connections of cells of the skin.

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There are several forms of hereditary epidermolysis bullosa. Some forms of the condition can be present at birth, while acquired forms occur in adults. Dystrophic epidermolysis bullosa present at birth is characterized by blistering, growing skin and mucous lesions. Adults suffering from the condition may have mitten-like deformities of fingers and toes. Epidermolysis bullosa is chronically debilitating and life-threatening.

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

At the time of designation, epidermolysis bullosa affected less than 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 23,000 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 submission of the application for the orphan drug designation there was no treatment authorised in the European Union. Treatment of epidermolysis bullosa included supportive care and antibiotics for the treatment of infections on the skin and, in some cases, surgery.

How is this medicine expected to work?

The bilayer engineered skin composed of keratinocytes (cells from the upper layer of the skin) from the patient (autologous) and fibroblasts (a fibroblast is a type of cell that synthesizes the extracellular matrix that acts as a frame around organs and gives them support) from a donor (allogeneic) embedded in a plasma matrix are expected to provide the missing collagen VII of the skin of patients with epidermolysis bullosa and thus prevent the formation of blisters.

What is the stage of development of this medicine?

The evaluation of the effects of bilayer engineered skin composed of keratinocytes from the patient (autologous) and fibroblasts from a donor (allogeneic) embedded in a plasma matrix in experimental models was ongoing.

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

Bilayer engineered skin composed of keratinocytes from the patient (autologous) and fibroblasts from a donor (allogeneic) embedded in a plasma matrix was not authorised anywhere worldwide for epidermolysis bullosa or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 5 April 2006 recommending the granting of this designation.

[*]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 25), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 468,900,000 (Eurostat 2006).

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

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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	Bilayered engineered skin composed of keratinocytes from the patient (autologous) and fibroblasts from a donor (allogeneic) embedded in a plasma matrix	Treatment of epidermolysis bullosa
Bulgarian	Конструирана двуслойна кожа, състояща се от кератиноцити от пациента (автоложни) и фибробласти от донор (алогенни), разположени в плазмена матрица	Лечение на булозна епидермолиза
Croatian	Dvoslojno uzgojena koža sastavljena od keratinocita pacijenta (autolognih) i fibroblasta donora (alogenih) ugrađenih u plazmatski matriks	Liječenje bulozne epidermolize
Czech	Dvouvrstvá umělá pokožka složená z keratinocytů od pacienta (autologních) a fibroblastů od dárce (allogenních) uložených v plazmovém lůžku	Léčba bulózní epidermolýzy
Danish	Tolaget, forarbejdet hud sammensat af keratinocytter fra patienten (autologe) og fibroblaster fra en donor (allogene) indlejret i en plasmamatrix	Behandling af epidermolysis bullosa
Dutch	Tweelagige geconstrueerde huid vervaardigd uit keratinocyten van de patiënt (autoloog) en fibroblasten van een donor (allogeen) verankerd in een plasmamatrix	Behandeling van epidermolysis bullosa
Estonian	Kahekihiline istutatud nahk, mis koosneb patsiendi keratinotsüütidest (autoloogsed) ja doonori fibroplastidest (allogeensed), asetatuna plasma maatriksisse	Bulloosse epidermolüüsi ravi
Finnish	Kaksikerroksinen keinotekoinen iho, joka koostuu plasmamatriksiin siirretyistä potilaan keratinosyyteistä (autologinen) ja luovuttajan fibroblasteista (allogeeninen)	Epidermolysis bullosan hoito
French	Bicouche de peau inginierisée composée de kératinocytes du patient (autologues) et de fibroblastes d'un donneur (allogéniques) inclus dans une matrice plasmatique	Traitement de l'épidermolyse bulleuse

[1] At the time of transfer of sponsorship

Language	Active Ingredient	Indication
German	Zweischichtige erstellte Haut,bestehend aus Keratinozyten vom Patienten(autolog) und Fibroblasten von einem Spender(allogenic) eingebettet in einer Plasmamatrix	Behandlung der Epidermolysis bullosa
Greek	Δέρμα δομημένο σε διπλή στοιβάδα συντιθέμενο από κερατινοκύτταρα ασθενούς (αυτόλογα) και ινωδοβλάστες από δότη (αλλογενετικά) εγκεκλεισμένα σε πλασματική βάση	Θεραπεία της πομφολυγώδους επιδερμόλυσης
Hungarian	A beteg keratinocitáiból (autológ) és a donor fibroblasztjaiból (allogén) álló, plazma mátrixba ágyazott kétrétegű mesterséges bőr	Epidermolysis bullosa kezelése
Italian	Pelle artificiale a doppio strato composta da cheratinociti del paziente (autologo) e fibroblasti di un donatore (allogenico) immersa in una matrice plasmatica	Trattamento della epidermolisi bollosa
Latvian	Plazmas matricē ievietota divu slāņu āda, kas veidota no pacienta keratinocītiem (autologs) un donora fibroblastiem (allogēns)	Bulozās epidermolīzes ārstēšanai
Lithuanian	Dvisluoksnė, sukonstruota oda sudaryta iš paciento (autologinių) keratinocitų ir donoro (alogeninių) fibroblastų, integruotų į plazminę matricą	Pūslinės epidermolizės gydymas
Polish	Dwuwarstwowa, sztuczna skóra, składająca się z keratynocytów pacjenta (autologicznych) oraz fibroblastów pochodzących od dawcy (allogenicznych), zatopionych w plazmatycznej macierzy	Pęcherzowe oddzielanie się naskórka
Portuguese	Bicamada de pele obtida por engenharia e composta por queratinócitos do doente (autologos) e por fibroblastos do dador (alogenicos) ligada numa matriz plasmatica	Tratamento da epidermolise bulhosa
Romanian	Piele în dublu strat realizată prin bioinginerie, compusă din keratinocite provenite de la pacient (autologe) şi fibroblaşti proveniţi de la un donator (alogeni), încorporate într-o matrice de plasmă	Tratamentul epidermolizei buloase
Slovak	Dvojvrstvová umelá koža tvorená keratinocytmi od pacienta (autológnymi) a fibroblastmi od darcu (alogénnymi) vložená v plazmatickom substráte	Liečba epidermolysis bullosa

Language	Active Ingredient	Indication
Slovenian	Z inženiringom ustvarjena dvoplastna koža, zgrajena iz keratinocitov pacienta (avtologni) in fibroblastov darovalca (alogenski) vloženih v plazemski matriks	Zdravljenje bulozne epidrmolize
Spanish	Bicapa de piel ingenierizada compuesta por queratinocitos del paciente (autólogos) y fibroblastos de un donante (alogénicos) embebidos en una matriz plasmática	Tratamiento de la epidermolisis bullosa
Swedish	Dubbel lager odlad hud bestående av keratinocyter från patienten (autologa) och fibroblaster från donator (allogena) omslutna i plasma matris	Behandling av epidermolysis bullosa
Norwegian	Hud konstruert som et dobbeltlag sammensatt av keratinocytter fra pasienter (autologe) og fibroblaster fra donor (allogene) innleiret I en plasmamatriks	Behandling av epidermolysis bullosa
Icelandic	Tveggja laga tilbúin húð samsett úr hyrnisfrumum úr sjúklingnum (samgena) og trefjakímfrumum úr gjafa (ósamgena) í plasma stoðgrind	Meðferð á epidermolysis bullosa