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Public summary of opinion on orphan designation

Genetically modified replication-incompetent herpes simplex virus-1 expressing collagen VII for treatment of epidermolysis bullosa

On 16 April 2018, orphan designation (EU/3/18/2012) was granted by the European Commission to IDEA Innovative Drug European Associates Limited, United Kingdom, for genetically modified replication-incompetent herpes simplex virus-1 expressing collagen VII (also known as KB103) for treatment of epidermolysis bullosa.

What is epidermolysis bullosa?

Epidermolysis bullosa is a group of inherited diseases 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 reduce life expectancy.

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

At the time of designation, epidermolysis bullosa affected 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).

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 517,400,000 (Eurostat 2018).

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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 intended for patients who have epidermolysis bullosa due to a mutation in the *COL7A1* gene. This gene normally produces a substance called collagen 7 that helps hold skin layers together.

The medicine is made of a virus that contains the normal *COL7A1* gene. When given to the patient, the virus is expected to carry the normal *COL7A1* gene into the patient's skin cells. The skin cells are then expected to produce collagen 7, correcting the cause of the condition and preventing blister formation.

The virus used in this medicine (herpes simplex) has been modified so that it does not cause disease in humans.

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 the US for dystrophic epidermolysis bullosa.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 15 March 2018 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	Genetically modified replication-incompetent herpes simplex virus-1 expressing collagen VII	Treatment of epidermolysis bullosa
Bulgarian	Генетично модифициран репликационно-некомпетентен херпес симплекс вирус-1, експресиращ колаген VII	Лечение на булозна епидермолиза
Croatian	Genetski modificiran herpes simplex virus-1 nesposoban za replikaciju koji eksprimira kolagen VII	Liječenje bulozne epidermolize
Czech	Geneticky modifikovaný replikační inkompetentní virus herpes simplex virus-1, který exprimuje kolagen VII	Léčba bulózní epidermolýzy
Danish	Genetisk modificeret replikationsinkompetent herpes simplex virus-1, der udtrykker collagen VII	Behandling af epidermolysis bullosa
Dutch	Genetisch gemodificeerde replicatie-incompetente herpes simplex virus-1 dat collageen VII tot expressie brengt	Behandeling van epidermolysis bullosa
Estonian	Kollageen VII ekspresseeriv geneetiliselt muundatud replikatsioonivõimetu Herpes simplex viirus 1 (HSV1)	Bulloosse epidermolüüsi ravi
Finnish	Geneettisesti muunneltu replikaatio inkompetentti herpes simplex virus-1, joka ilmentää kollageeni VII:ää	Epidermolysis bullosan hoito
French	Virus-1 de l'herpès simplex génétiquement modifié et incapable de réplication qui exprime le collagène VII	Traitement de l'épidermolyse bulleuse
German	Genetisch modifiziertes replikationsinkompetentes Herpes Simplex Virus-1, das Kollagen VII exprimiert	Behandlung der Epidermolysis bullosa
Greek	Γενετικά τροποποιημένος ιός απλού έρπητα-1 που εκφράζει κολλαγόνο VII	Θεραπεία της πομφολυγώδους επιδερμόλυσης
Hungarian	Kollagén VII-et expresszáló, genetikailag módosított replikáció-inkompetens herpes simplex virus-1	Epidermolysis bullosa kezelése
Italian	Herpes simplex virus-1 geneticamente modificato, replicazione- incompetente, che esprime collagene VII	Trattamento della epidermolisi bollosa
Latvian	Ģenētiski modificēts replicēties nespējīgs herpes simplex vīruss-1, kas ekspresē kolagēnu VII	Bulozās epidermolīzes ārstēšanai
Lithuanian	Genetiškai modifikuotas nesugebantis replikuoti herpes simplex virusas-1, ekspresuojantis kolageną VII	Pūslinės epidermolizės gydymas
Maltese	Replikazzjoni ġenetikament modifikata-herpes simplex virus-1 inkompetenti li jesprimi l-kollaġen VII	Kura tal-epidermolisi bullosa
Polish	Genetycznie zmodyfikowany niezdolny do replikacji wirus herpes simplex-1, wyrażający kolagen VII	Pęcherzowe oddzielanie się naskórka
Portuguese	Herpes-vírus simples 1 modificado geneticamente para conferir a incompetência de replicação e a expressão do colagénio VII	Tratamento da epidermólise bulhosa
Romanian	Virus herpes simplex de tip 1 modificat genetic incompetent pentru replicare care exprimă colagenul VII	Tratamentul epidermolizei buloase

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Geneticky modifikovaný replikačne nekompetentný vírus herpes simplex-1, ktorý exprimuje kolagén VII	Liečba epidermolysis bullosa
Slovenian	Genetsko modificiran in nesposoben replikacije herpes simplex virus-1, ki izraža kolagen VII	Zdravljenje bulozne epidrmolize
Spanish	Virus de herpes simple-1 incompetente genéticamente modificado que expresa colágeno VII	Tratamiento de la epidermolisis bullosa
Swedish	Genetiskt modifierat replikationsinkompetent herpes simplex virus-1 som uttrycker kollagen VII	Behandling av epidermolysis bullosa
Norwegian	Genetisk modifisert replikasjon-inkompetent herpes simplex virus-1 som uttrykker kollagen VII	Behandling av epidermolysis bullosa
Icelandic	Erfðabreyttar afritunar-ófullnægjandi herpes simplex veira-1 sem tjáir kollagen VII	Meðferð á epidermolysis bullosa