12 October 2017
EMA/690435/2017

Public summary of opinion on orphan designation

Antisense oligonucleotide targeting exon 73 in the *COL7A1* gene for the treatment of epidermolysis bullosa

On 12 October 2017, orphan designation (EU/3/17/1938) was granted by the European Commission to ProQR Therapeutics VII BV, the Netherlands, for antisense oligonucleotide targeting exon 73 in the *COL7A1* gene (also known as QR-313) for the 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 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 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.

[*]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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How is this medicine expected to work?

The 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. In patients with the mutation, the gene cannot produce working collagen 7.

The medicine is an 'antisense oligonucleotide', a small strand of synthetic genetic material. It has been designed to attach to the mutated area of the *COL7A1* gene in skin cells, and to allow production of a shortened but working form of collagen 7. Applying the medicine to the skin is expected to result in improvement in the symptoms of the condition.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

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 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 5 October 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	Antisense oligonucleotide targeting exon 73 in the *COL7A1* gene	Treatment of epidermolysis bullosa
Bulgarian	Антисенс олигонуклеотид насочен към екзон 73 на *COL7A1* гена	Лечение на булозна епидермолиза
Croatian	Protusmjeri oligonukleotid koji cilja egzon 73 u genu *COL7A1*	Liječenje bulozne epidermolize
Czech	Antisense oligonukleotid zacílený na exon 73 v *COL7A1* genu	Léčba bulózní epidermolýzy
Danish	Antisensoligonukleotid rettet mod exon 73 i *COL7A1*-genet	Behandling af epidermolysis bullosa
Dutch	Antisense oligonucleotide gericht tegen exon 73 in het *COL7A1* gen	Behandeling van epidermolysis bullosa
Estonian	*COL7A1* geeni 73. eksonit sihtiv *antisense* oligonukleotiid	Bulloosse epidermolüüsi ravi
Finnish	Antisense-oligonukleotidi, jonka kohteena on *COL7A1*-geenin eksoni 73	Epidermolysis bullosan hoito
French	Oligonucléotide antisens ciblant l'exon 73 du gène *COL7A1*	Traitement de l'épidermolyse bulleuse
German	Antisense-Oligonukleotid, das auf Exon 73 des *COL7A1* Gens abzielt	Behandlung der Epidermolysis bullosa
Greek	Αντινοηματικό νουκλεοτίδιο που στοχεύει το εξόνιο 73 του γονιδίου *COL7A1*	Θεραπεία της πομφολυγώδους επιδερμόλυσης
Hungarian	A *COL7A1* gén 73-as exonját célzó antiszenz oligonukleotid	Epidermolysis bullosa kezelése
Italian	Oligonucleotide antisenso contro l'esone 73 del gene *COL7A1*	Trattamento della epidermolisi bollosa
Latvian	Antisensa oligonukleotīds, kas vērsts pret *COL7A1* gēna 73. eksonu	Bulozās epidermolīzes ārstēšanai
Lithuanian	Priešprasmis oligonukleotidas nukreiptas į *COL7A1* geno 73 egzoną	Pūslinės epidermolizės gydymas
Maltese	Antisensi oligonukleotide li għandu fil-mira eżon 73 fil-ġene *COL7A1*	Kura tal-epidermolisi bullosa
Polish	Antysensowny oligonukleotyd nakierowany przeciw eksonowi 73 genu *COL7A1*	Pęcherzowe oddzielanie się naskórka
Portuguese	Oligonucleotídeo anti-senso direcionado para o exão 73 no gene *COL7A1*	Tratamento da epidermólise bulhosa
Romanian	Oligonucleotidă antisens ţintind exonul 73 al genei *COL7A1*	Tratamentul epidermolizei buloase
Slovak	Antisense oligonukleotid zacielený na exon 73 v *COL7A1* géne	Liečba epidermolysis bullosa

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Protismerni oligonukleotid, usmerjen v ekson 73 gena *COL7A1*	Zdravljenje bulozne epidrmolize
Spanish	Oligonucleótido antisentido dirigido al exón 73 en el gen *COL7A1*	Tratamiento de la epidermolisis bullosa
Swedish	Antisensoligonukleotid riktad mot exon 73 i *COL7A1*-genen	Behandling av epidermolysis bullosa
Norwegian	Antisense oligonukleotid rettet mot exon 73 i genet for *COL7A1*	Behandling av epidermolysis bullosa
Icelandic	Antisense ólígónúkleótíð sem beinist gegn exon 73 í *COL7A1* geni	Meðferð á epidermolysis bullosa