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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human transglutaminase 1 encapsulated into liposomes for the treatment of transglutaminase-1-deficient autosomal recessive congenital ichthyosis

On 7 June 2013, orphan designation (EU/3/13/1130) was granted by the European Commission to Westfälische Wilhelms-Universität Münster, Germany, for recombinant human transglutaminase 1 encapsulated into liposomes for the treatment of transglutaminase-1-deficient autosomal recessive congenital ichthyosis.

What is transglutaminase-1-deficient autosomal recessive congenital ichthyosis?

Transglutaminase-1-deficient autosomal recessive congenital ichthyosis is an inherited skin disorder caused by abnormalities in a gene called *TGM1*, which produces the enzyme transglutaminase-1. This enzyme is important for normal formation of the outer layer of the skin. The main feature of the disorder is dry, thick, scaly or flaky skin. In its most severe form, children are born prematurely and have problems such as dehydration and difficulties in maintaining a normal body temperature.

Transglutaminase-1-deficient autosomal recessive congenital ichthyosis is a long-term debilitating disease due to the appearance of symptoms at birth or in early childhood. It can cause life-threatening complications in new born babies including breathing and feeding problems and infections.

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

At the time of designation, transglutaminase-1-deficient autosomal recessive congenital ichthyosis affected approximately 0.04 in 10,000 people in the European Union (EU). This was equivalent to a total of around 2,000 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 27), Norway, Iceland and Liechtenstein. This represents a population of 509,000,000 (Eurostat 2013).

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What treatments are available?

At the time of designation, acitretin was authorised in some countries of the EU to treat autosomal recessive congenital ichthyosis. In addition, basic measures to manage patients with this condition included mechanical scale removal and moisturising of the underlying skin.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with transglutaminase-1-deficient autosomal recessive congenital ichthyosis because studies in experimental models show that it helps restore a more normal structure in the skin of patients with this condition. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Patients with transglutaminase-1-deficient autosomal recessive congenital ichthyosis lack an enzyme called transglutaminase-1. This medicine is expected to be available as a cream that contains the transglutaminase-1 enzyme as its active substance. Transglutaminase-1 is contained within tiny fatty particles called liposomes, which are expected to carry the enzyme through the skin. This is expected to help restore the normal formation of the outer layer of the skin.

The transglutaminase-1 in this medicine is made by a method known as 'recombinant DNA technology': it is made by cells into which a gene (DNA) has been introduced that makes them able to produce the enzyme.

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 this medicine in experimental models was ongoing.

At the time of submission, no clinical trials with the medicine in patients with transglutaminase-1-deficient autosomal recessive congenital ichthyosis had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for transglutaminase-1-deficient autosomal recessive congenital ichthyosis 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 17 April 2013 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:

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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	Recombinant human transglutaminase 1 encapsulated into liposomes	Treatment of transglutaminase-1-deficient autosomal recessive congenital ichthyosis
Bulgarian	Рекомбинирана човешка трансглутаминаза 1 капсулирана в липозоми	Лечение на автозомно-рецесивна вродена ихтиоза в следствие на трансглутаминаза 1 дефицит
Czech	Rekombinantní lidská transglutamináze 1 zapouzdřeny do lipozomů	Léčba autozomálně recesivní kongenitální ichtyózy způsobené deficitem transglutamináznízní 1
Danish	Rekombinant human transglutaminase 1 indkapslet i liposomer	Behandling af autosomal recessiv medfødt iktyose som skyldes transglutaminase 1 mangel□
Dutch	Recombinant humaan transglutaminase 1 ingekapseld in liposomen	Behandeling van transglutaminase 1-deficiënte autosomaal recessieve congenitale ichthyosis
Estonian	Rekombinantne inimese transglutaminaas 1 kapseldatuna liposoomidesse	Transglutaminaasi 1 defitsiidist tingitud kaasasündinud autosoom-retsessiivse ihtüoosi ravi
Finnish	Rekombinantti ihmisen transglutaminaasi 1 kapseloituna liposomeihin	Peittyvästi periytyvän synnynnäisen, transglutaminaasi 1:n puutteesta johtuvan iktyoosin hoito
French	Transglutaminase 1 recombinante humaine encapsulée dans des liposomes	Traitement de l'ichtyose congénitale autosomal récessive due à la déficience en transglutaminase 1
German	Rekombinante humane Transglutaminase 1 eingekapselt in Liposomen	Behandlung der Transglutaminase 1 defizienten autosomal rezessiven kongenitalen Ichthyose
Greek	Ανασυνδυασμένη ανθρώπινη τρανσγλουταμινάση 1 έγκλειστη σε λιποσώματα	θεραπεία αυτοσωματικής υπολειπόμενης ιχθύωσης λόγω εκ γενετής έλλειψης της τρανσγλουταμινάσης 1
Hungarian	Liposzómába zárt rekombináns humán transzglutamináz-1	Transzglutamináz-1 hiány okozta autoszomális recesszív veleszületett ichthyosis kezelése
Italian	Transglutaminasi 1 ricombinante umana incapsulata nei liposomi	Trattamento dell'ittiosi autosomica recessiva congenita causata dalla carenza di transglutaminasi 1
Latvian	Rekombinēta cilvēka transglutamināze 1 iekapsulēta liposomās	Iedzimtas autosomāli recesīvās transglutamināzes 1 deficīta ihtiozes ārstēšana
Lithuanian	Liposomose inkapsuliuota rekombinantinė žmogaus transgliutaminazė 1	Autosominės recesyvinės įgimtos ichtiozės, trūkstant transgliutaminazės 1, gydymas

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	Transglutaminase 1 uman rikombinanti inkapsulati fl liposomi	Kura ta' ittjosi konġenitali awtosomali reċessiva minħabba nuqqas ta' transglutaminase 1
Polish	Rekombinowana ludzka transglutaminaza 1 w liposomach	Leczenie autosomalnej recesywnie dziedziczonej wrodzonej rybiej łuski wywołanej niedoborem transglutaminazy 1
Portuguese	Transglutaminase 1 humana recombinante encapsulada em lipossomas	Tratamento da ictiose autossómica recessiva congénita por deficiência de transglutaminase 1
Romanian	Transglutaminază 1 recombinantă umană încapsulată în lipozomi	Tratamentul ihtiozei congenitale autosomal recesive produse de deficitul de transglutaminază 1
Slovak	Rekombinantná ľudská transglutamináza 1 enkapsulovaná v lipozómoch	Liečba autozomálne recesívnej vrodenej ichtyózy spôsobenej nedostatkom transglutaminázy 1
Slovenian	Rekombinantna humana transglutaminaza 1, inkapsulirana v liposome	Zdravljenje avtosomno recesivne prirojene ihtioze zaradi pomanjkanja transglutaminase 1
Spanish	Transglutaminasa 1 recombinante humana encapsulada en liposomas	Tratamiento de la ictiosis congénita autosómica recesiva por deficiencia de transglutaminasa-1
Swedish	Rekombinant mänskligt transglutaminas 1 inkapslat i liposomer	Behandling av autosomal recessiv kongenital iktyos med transglutaminas 1 brist
Norwegian	Rekombinant human transglutaminase 1 innkapslet i liposomer	Behandling av autosomal recessiv medfødt iktyose som skyldes transglutaminase 1-mangel
Icelandic	Manna raðbrigða transglútamínasa 1 pakkað í lípósómum	Meðferð á autósómal víkjandi meðfæddu ichthýósis sem stafar af transglútamínasa-1- skorti