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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

human immunoglobulin G1 constant region - human ectodysplasin-A1 receptor-binding domain fusion protein for the treatment of X-linked hypohidrotic ectodermal dysplasia (Christ-Siemens-Touraine Syndrome)

On 14 December 2005, orphan designation (EU/3/05/334) was granted by the European Commission to Mr Eric Lucien, France, for human immunoglobulin G1 constant region - human ectodysplasin-A1 receptor-binding domain fusion protein for the treatment of X-linked hypohidrotic ectodermal dysplasia (Christ-Siemens-Touraine Syndrome).

The sponsorship was transferred to Apoxis (UK) Ltd, United Kingdom, in August 2006 and subsequently to Edimer Ltd, United Kingdom, in November 2009.

What is X-linked hypohidrotic ectodermal dysplasia (Christ-Siemens-Touraine Syndrome)?

Initially, the human embryo is made of three layers of cells (ectoderm, mesoderm and endoderm). Each layer will then proceed to further differentiate (the process cells undergo as they progress into mature cells) into organs and tissues specific for that particular layer. The ectoderm gives rise to the epidermis (e.g. the upper layer of the skin, sweat glands, breast glands, hair and nails and a part of the mouth) and neural tissue (e.g. the nerves, brain tissue). X-linked hypohidrotic ectodermal dysplasia (Christ-Siemens-Touraine Syndrome) is a hereditary disease characterised by an abnormal development of the organs and tissues derived from the ectoderm. Genes located on structures present in each cell of the body (the chromosomes), carry the genetic information that determines the characteristics of each individual. In humans, the so-called X and Y-chromosomes determine the sex, but carry also other genetic information. X-linked hypohidrotic ectodermal dysplasia (Christ-Siemens-Touraine Syndrome) is caused by an abnormality of a gene located on the X chromosome. This gene is responsible for the production of a protein, ectodysplasin-A1, that induces a series of actions needed to develop the ectoderm layer into the different mature normal cells and tissues. This protein is missing in patients affected by the condition. As boys, contrary to girls, only have one single copy of chromosome X, thus one single copy of this gene, they have much higher probabilities of suffering from the syndrome.

Patients affected by the condition cannot control their body temperature through sweating, lack normal hair, have an abnormal development of their mouth and teeth, etc. X-linked hypohidrotic ectodermal

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dysplasia (Christ-Siemens-Touraine Syndrome) is a life-threatening disease that increases the risk of death.

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

At the time of designation, X-linked hypohidrotic ectodermal dysplasia (Christ-Siemens-Touraine Syndrome) affected less than 0.1 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of fewer than 4,600 people, and is below the threshold 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?

There is at present no satisfactory treatment that has been authorised in the Community for patients affected by the condition.

How is this medicine expected to work?

Human immunoglobulin G1 constant region - human ectodysplasin-A1 receptor-binding domain fusion protein is a protein with two components: the first part is a part of a human immunoglobulin (immunoglobulins are specific proteins that play an important role in the defence mechanism) and is necessary to maintain the funcional structure of the product, while the second part is the part of the lacking protein in Christ-Siemens-Touraine Syndrome. The product is expected to replace the lacking protein ectodysplasin-A1 and to be able to induce the normal development of the tissues deriving from the ectoderm.

What is the stage of development of this medicine?

The effects of human immunoglobulin G1 constant region - human ectodysplasin-A1 receptor-binding domain fusion protein were evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials in patients with X-linked hypohidrotic ectodermal dysplasia (Christ-Siemens-Touraine Syndrome) were initiated.

The medicinal product was not authorised anywhere worldwide for X-linked hypohidrotic ectodermal dysplasia (Christ-Siemens-Touraine Syndrome) or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 24 October 2005 a positive opinion recommending the grant of the above-mentioned designation.

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;

[*]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. This represents a population of 459,700,000 (Eurostat 2004).

- either the rarity of the condition (affecting not more than 5 in 10,000 people in the European Union) 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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Translations of the active ingredient and indication in all official EU languages, Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Human immunoglobulin G1 constant region – human ectodysplasin-A1 receptor-binding domain fusion protein	Treatment of X-linked hypohidrotic ectodermal dysplasia (Christ-Siemens-Touraine Syndrome)
Czech	Konstantní oblast lidského imunoglobulinu G1 – fúzní protein receptorové vazebné domény lidského ektodysplasinu-A1	Léčba hypohidrotické ektodermální dysplazie vázané na chromozom X (Christ-Siemens-Touraine syndrom)
Danish	Humant immunglobulin G1-konstantregion – humant ectodysplasin-A1 receptorbindende domæne-fusionsprotein	Behandling af X-bundet hypohidrotisk ektodermal dysplasi (Christ-Siemens-Touraine syndrom)
Dutch	Humaan immunoglobuline G1 constant deel – humaan ectodysplasine-A1 receptorbindend domeinfusie-eiwit	Behandeling van X-gerelateerde hypohidrotische ectodermale dysplasie (Christ-Siemens-Touraine syndroom)
Estonian	Inimese immunoglobuliini G1 konstantne piirkond – inimese ektodüsplasiin-A1 retseptoriga siduva domeeni liitvalk	X-liitelise hüpohidrootilise ektodermaalse düsplaasia (Christ-Siemens-Touraine sündroomi) ravi
Finnish	Ihmisperäinen immunoglobuliini G1 vakio alue – ihmisperäinen ektodysplasiini-A1 reseptoreja sitova alueellinen fuusio-proteiini	x-linkittyneen hypohidroottisen ektodermaalisen dysplasian hoito (Christ-Siemens-Touraine syndrooma)
French	Protéine de fusion de la région constante de l'immunoglobuline G1 humaine –au site de liaison du récepteur à l'ectodysplasine humaine A1	Traitement des dysplasies ectodermiques anhidrotiques liées au chromosome X (Syndrome de Christ-Siemens-Touraine)
German	Human-Immunoglobulin G1 konstante Region – Human-Ektodysplasin-A1 rezeptorbindendes Domäne Fusionsprotein	Behandlung der X-chromosomal assoziierten hypohidrotischen ektodermalen Dysplasie (Christ-Siemens-Touraine Syndrome)

Language	Active Ingredient	Indication
Greek	Δραστική ουσία - Ανθρώπινη άνοση γ-σφαιρίνη G1 σταθερού τμήματος - ανθρώπινη εκτοδυσπλασίνη-A1 πρωτεΐνη σύντηξης σύνδεσης με υποδοχέα	Θεραπεία της φυλοσύνδετης υπο-ιδρωτικής εξωδερμικής δυσπλασίας (Christ-Siemens-Touraine Syndrome)
Hungarian	Humán immunoglobulin G1 konstans szakasz – humán ectodysplasin-A1 receptor-kötő domain fúziós fehérje	X-kromoszómához kötött hypohidrotikus ektodermális dysplasia kezelése (Christ-Siemens-Touraine szindróma)
Italian	Proteina di fusione della regione costante dell'immunoglobulina umana G1 con il dominio di legame del recettore dell'ectodisplasina-A1 umana	Trattamento della displasia ectodermica ipoidrotica X-linked (Sindrome di Christ-Siemens-Touraine)
Latvian	Cilvēka imūnglobulīna G1 pastāvīgs apvidus - cilvēka ektodisplazīna-A1 receptorus saistošs savienošanās proteīna domēns	Ar X hromosomu saistītas hipohidrotiskās ektodermālās displāzijas (Christ-Siemens-Touraine sindroma) ārstēšanai
Lithuanian	Žmogaus imunoglobulino G1 nekintanti dalis – žmogaus ektodisplazin-A1 receptorius surišantis domeno sintezės baltymas	Su X chromosoma susijusios hipohidrinės ektoderminės displazijos (Christ-Siemens-Touraine sindromas) gydymas
Polish	Stały region ludzkiej immunoglobuliny G1 - białka łączącego domenę wiążącą receptora dla ludzkiej ektodysplazyny A1	Leczenie hipohydrotycznej dysplazji ektodermalnej związanej z chromosomem X (Zespół Christ-Siemens-Tourain'a)
Portuguese	Proteína de fusão do domínio de ligação de receptores de imunoglobulina humana G1 de fracção constante– ectodisplasina A1 humana	Tratamento da displasia ectodérmica hipoidrótica ligada ao cromossoma X (síndrome de Christ-Siemens-Touraine)
Slovak	Konštantná oblasť ľudského imunoglobulínu G1 - fúzny proteín receptorovej väzobnej domény ľudského ektodysplasínu-A1	Liečba hypohidrotickej ektodermálnej dysplázie viazanej na chromozóm X (Syndróm Christ-Siemens-Touraine)
Slovenian	Odlomek Fc humanega imunoglobulina G1 – beljakovina, ki se veže na receptor humanega ektodisplazina A1	Zdravljenje hipohidrotične na X-kromosom vezane ektodermalne displazije (Sindrom Cerest-Siemens-Touraine)

Language	Active Ingredient	Indication
Spanish	Región constante de la inmunoglobulina G1 humana – proteína de fusión con un dominio de unión al receptor de la ectodisplasina A1 humana	Tratamiento de la displasia ectodérmica hipohidrótica (DEH) ligada al sexo (síndrome de Christ-Siemens-Touraine)
Swedish	Humant immunoglobulin G1 konstant region – humant ektodysplasin A receptorbindande domänfusionsprotein	Behandling av X-kromosombundet hypohidrotisk ektodermal dysplasi (Christ-Siemens-Touraine Syndrome)
Norwegian	Humant immunoglobulin G1 konstant region - humant ektodysplasin-A1 reseptorbindende domenefusjonsprotein	Behandling av X-bundet hypohidrotisk ektodermal dysplasi (Christ-Siemens-Touraine syndrom)
Icelandic	Mannaónæmisglóbúlín G1 fastasvæði – manna ektódýsplasín-A1 viðtakabindandi hneppissamrunaprótín	Meðferð á X-tengdri óeðlilegri minnkun á svitamyndun (Christ-Siemens-Touraine heilkenni)