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EMA/COMP/77786/2004
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human insulin-like growth factor-I/recombinant human insulin-like growth factor binding protein-3 for the treatment of Type A extreme insulin resistance syndrome

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in May 2007 on request of the sponsor.

On 21 October 2004, orphan designation (EU/3/04/236) was granted by the European Commission to Insmed Incorporated, United Kingdom, for recombinant human insulin-like growth factor-I/recombinant human insulin-like growth factor binding protein-3 (rhIGF-I/rhIGFBP-3) for the treatment of Type A extreme resistance insulin syndrome.

The sponsorship was transferred to Insmed Europe Ltd, United Kingdom, in December 2006.

What is Type A extreme insulin resistance syndrome?

Insulin is a hormone that helps the body break down the sugar in the food to use as energy. Normally, sugar does not accumulate in the blood in excess. Insulin binds to insulin-receptors on the surface of cells and the sugar is then taken up by the cells. Type A extreme insulin resistance syndrome is due to an inherited condition where the insulin receptors are not produced normally. This means that insulin cannot properly bind to the receptors causing sugar to accumulate in the blood. In patients, this appears as high levels of insulin in the blood (hyperinsulinaemia), increased colouration and "velvety" thickening (acanthosis nigricans) of the skin and development of male-like features in females (virilisation). Type A extreme insulin resistance syndrome is a chronically debilitating condition.

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

At the time of designation, Type A extreme insulin resistance syndrome affected approximately 0.02 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 900 people, and is

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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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?

Several methods of treatment such as insulin, oral antidiabetic medicines alone or in combination have been used although there exist no authorised therapeutic method.

How is this medicine expected to work?

The product may work by going around the abnormal pathway represented by insulin and its defective receptor. Recombinant human insulin-like growth factor-I/recombinant human insulin-like growth factor binding protein-3 (rhIGF-I/rhIGFBP-3) is a complex formed by two parts: recombinant human insulin-like growth factor and its binding protein. Recombinant human insulin-like growth factor shares structural and functional similarities with insulin. It can produce its insulin-like functions by binding to its own receptors although it can bind to insulin receptors. The role of the binding protein is to reduce the insulin-like side effects such as hypoglycaemia, in addition to other functions as carrier of insulin-like growth factor-I.

What is the stage of development of this medicine?

The effects of rh IGF-I/rh IGF-IBP3 has been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials in patients with Type A extreme insulin resistance were initiated.

RhIGF-I/rhIGFBP-3 has been granted orphan drug status in the United States for the treatment of Growth Hormone Insensitivity Syndrome and the treatment of Extreme Insulin Resistance Syndrome. Recombinant human insulin-like growth factor-I/recombinant human insulin-like growth factor binding protein-3 (rhIGF-I/rhIGFBP-3) has been granted orphan drug status in the United States on December 9, 2003 for the treatment of Extreme Insulin Resistance Syndrome (Type A syndrome , Rbason-Mendenhall syndrome, Leprechaunism and Type B syndrome).

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 September 2004 recommending the granting of this 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;
- 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 insulin-like growth factor-I /recombinant human insulin-like growth factor binding protein-3	Treatment of Type A extreme insulin resistance syndrome
Czech	Rekombinantní lidský růstový faktor-I podobný inzulinu/ rekombinantní lidský růstový faktor vážící protein-3' podobný inzulínu	Léčba syndromu inzulínové resistencetypu A
Danish	Recombinant human insulin - ligende vækst faktor - I recombinant human insulin - ligende vækst faktor bindende protein -3	Behandling af type A ekstrem insulinresistenssyndrom
Dutch	Recombinant humaan insuline-achtige groei factor-I/recombinant humaan insuline-achtige groeifactor bindend proteïne-3	Behandeling van type A extreem insulineresistentiesyndroom
Estonian	Rekombinantne inimese insuliinitaoline kasvufaktor-1 /rekombinantne inimese insuliinitaolist kasvufaktorit siduv valk-3	A tüüpi tugeva insuliiniresistentsuse sündroomi ravi
Finnish	Rekombinantin ihmis-insuliinin kaltainen kasvutekijä–I/rekombinantti ihmis-insuliinin kaltainen kasvutekijää sitova proteiini-3	Erittäin vakavan tyypin A insuliiniresistenssi-oireyhtymän hoito
French	Facteur de croissance insulinomimétique recombinant de type I / Facteur de croissance insulinomimétique recombinant lié à la protéine 3	Traitement des syndromes d'insulino-résistance extrême de type A
German	Recombinantes humanes Insulin-wie Wachstumsfactor -I/recombinantes humanes Insulin-wie Wachstumfaktor, der protein-3 bindet	Behandlung von Typ A extremem Insulinresistenz-Syndrom
Greek	Ανασυνδυαζόμενος ανθρώπινος αυξητικός παράγοντας ομοιάζων με ινσουλίνη /ανασυνδυαζόμενη δέσμευτική πρωτεΐνη 3 του ανθρώπινου αυξητικού παράγοντα ομοιάζοντος με ινσουλίνη	Θεραπεία των ακραίων συνδρομών αντοχής στην ινσουλίνη τύπου Α
Hungarian	Rekombináns humán inzulinszerű növekedési fak-tor-I/rekombináns humán inzulinszerű növekedési faktort kötő fehérje-3	A-típusú extrém inzulinrezisztencia szindróma kezelése

[1] At the time of designation

Language	Active Ingredient	Indication
Italian	Fattore di crescita ricombinante umano insulino-simile I/ proteina ricombinante umana legante il fattore di crescita insulino-simile 3	Trattamento della sindrome da insulino-resistenza estrema di tipo A
Latvian	Rekombinantais cilvēka insulīnam līdzīgais augšanas faktors-i/rekombinanto cilvēka insulīnam līdzīgo augšanas faktoru saistošais proteīns-3	A tipa galēji smagas insulīna rezistences sindroma ārstēšana
Lithuanian	Rekombinantinis žmogaus į insuliną panašus augimo faktorius I/rekombinantinis žmogaus į insuliną panašus augimo faktorius, susijęs su baltymu-3	Ypač sunkaus atsparumo insulinui A tipo sindromo gydymas
Maltese	Recombinant human insulin-like growth factor-I /recombinant human insulin-like growth factor binding protein-3	Treatment of Type A extreme insulin resistance syndrome
Polish	Rekombinowany ludzki-insulinopodobny czynnik wzrostu-I /białko-3' wiążące rekombinowany ludzki insulinopodobny czynnik wzrostu	Leczenie krańcowego zespołu insulinooporności typu A
Portuguese	Factor de crescimento análogo à insulina – I humano recombinante/proteína ligante do factor de crescimento análogo à insulina – 3 humana recombinante	Tratamento do síndromas de Tipo A de resistência extrema à insulina
Slovak	Rekombinantný ľudský rastový faktor podobný inzulínu I / rekombinantný ľudský rastový faktor podobný inzulínu viažuci proteín 3'	Liečba extrémneho syndrómu inzulínovej rezistencie typu A
Slovenian	Rekombinantni človeški, inzulinu podobni rastni faktor-I/protein, ki se veže na rekombinantni človeški, inzulinu podobni rastni faktor-3	Zdravljenje hudega sindroma insulinske resistence vrste A
Spanish	Factor de crecimiento-I similar a la insulina recombinante humano / proteína de unión al factor de crecimiento similar a la insulina-3 recombinante humano	Tratamiento del síndrome tipo A de resistencia extrema a la insulina.
Swedish	Recombinant human insulin-lik tillväxtfaktor I/ recombinant human insulin-lik tillväxtfaktor bindingsprotein-3	Behandling av typ A extrem insulinresistens
Norwegian	Rekombinant human insulinlignende vekstfaktor-I /protein-3' som binder rekombinant human insulinlignende vekstfaktor	Behandling av type A ekstrem insulinresistenssyndrom

Language	Active Ingredient	Indication
Icelandic	Raðbrigða insúlínlíkur vaxtarþáttur-I úr mönnum / prótein-3 sem bindur raðbrigða insúlínlíkan vaxtarþátt úr mönnum	Meðferð við alvarleguinsúlínþolsheilkenni af tegund A