



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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 leprechaunism

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in March 2007 on request of the sponsor.

On 21 October 2004, orphan designation (EU/3/04/238) was granted by the European Commission to Insméd 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 leprechaunism.

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

What is leprechaunism?

Insulin is a hormone that helps the body use the sugar in the food as fuel. Because of the action of insulin, sugar does not normally accumulate in the blood in excess. In order to show its effects, insulin binds to insulin-receptors on cells' surface. Leprechaunism is an inherited disorder in which insulin cannot bind to insulin-receptors and therefore cannot function properly. Due to this defect there is a delay in the normal development occurring before and after birth. This delay is associated with characteristic facial features (resembling that of 'leprechauns', the ancient elves in the Irish folk traditions), reduction of the fatty and muscular tissues in the body. Signs of virilisation (male-like characters) are often observed in little girls. Imbalance in the sugar (glucose) level in the blood is also present. The condition is life-threatening.

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

At the time of designation, leprechaunism affected not more than 0.02 in 10,000 people in the European Union (EU)*. This is equivalent to a total of not more than/ fewer than 920 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).



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?

There was no authorised method of treatment at the time of designation. Treatment with recombinant human insulin-like growth factor (IGF) I had been used.

How is this medicine expected to work?

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 components: recombinant human insulin-like growth factor and its binding protein. As rhIGF-I is able to induce metabolic activities of insulin through IGF-I receptor, it is expected that the product will be able to bypass defects in the insulin receptor or insulin signalling pathway that are present in patients with Leprechaunism. Therefore the product is expected to reduce the symptoms and the growth retardation seen in these patients.

What is the stage of development of this medicine?

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

At the time of submission of the application for orphan designation, no clinical trials in patients with leprechaunism were initiated.

Recombinant human insulin-like growth factor-I/recombinant human insulin-like growth factor binding protein-3 (rhIGF-I/rhIGFBP-3) had 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 languages¹, 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 Leprechaunism
Czech	Rekombinantní lidský růstový faktor-I podobný inzulinu/ rekombinantní lidský růstový faktor vážící protein-3' podobný inzulinu	Léčba Leprechaunismus
Danish	Recombinant human insulin - ligende vækst faktor - I recombinant human insulin - ligende vækst faktor bindende protein -3	Behandling af leprechaunismus
Dutch	Recombinant humaan insuline-achtige groei factor-I/recombinant humaan insuline-achtige groeifactor bindend proteïne-3	Behandeling van Leprechaunisme
Estonian	Rekombinantne inimese insuliinitaoline kasvufaktor-1 / rekombinantne inimese insuliinitaolist kasvufaktorit siduv valk-3	Leprekhaunismi ravi
Finnish	Rekombinantin ihmis-insuliinin kaltainen kasvutekijä-I/rekombinantti ihmis-insuliinin kaltainen kasvutekijää sitova proteiini-3	Leprekaunismin hoito
French	Facteur de croissance insulino-mimétique recombinant de type I / Facteur de croissance insulino-mimétique recombinant lié à la protéine 3	Traitement du lepréchaunisme
German	Recombinantes humanes Insulin-wie Wachstumsfaktor -I/recombinantes humanes Insulin-wie Wachstumsfaktor, der protein-3 bindet	Behandlung von Leprechaunismus
Greek	Ανασυνδυαζόμενος ανθρώπινος αυξητικός παράγοντας ομοιάζων με ινσουλίνη /ανασυνδυαζόμενη δέσμευτική πρωτεΐνη 3 του ανθρώπινου αυξητικού παράγοντα ομοιάζοντος με ινσουλίνη	Θεραπεία του λεπρεχωνισμού
Hungarian	Rekombináns humán inzulinszerű növekedési fak-tor-I/rekombináns humán inzulinszerű növekedési faktort kötő fehérje-3	Leprechianismus kezelése
Italian	Fattore di crescita ricombinante umano insulino-simile I/ proteina ricombinante umana legante il fattore di crescita insulino-simile 3	Trattamento del leprecaunismo
Latvian	Rekombinantais cilvēka insulīnam līdzīgs augšanas faktors-i/rekombinanto cilvēka insulīnam līdzīgo augšanas faktoru saistošais proteīns-3	Donohjū sindroma ārstēšana

¹ At the time of designation

Language	Active Ingredient	Indication
Lithuanian	Rekombinantinis žmogaus į insuliną panašus augimo faktorius I/rekombinantinis žmogaus į insuliną panašus augimo faktorius, susijęs su baltymu-3	Leprečauizmo gydymas
Maltese	Recombinant human insulin-like growth factor-I / recombinant human insulin-like growth factor binding protein-3	Treatment of Leprechaunism
Polish	Rekombinowany ludzki-insulinopodobny czynnik wzrostu-I / białko-3' wiążące rekombinowany ludzki insulinopodobny czynnik-wzrostu	Leczenie leprechaunizmu
Portuguese	Factor de crescimento análogo à insulina – I humano recombinante/proteína ligante do factor de crescimento análogo à insulina – 3 humana recombinante	Tratamento do leprechaunismo
Slovak	Rekombinantný ľudský rastový faktor podobný inzulínu I / rekombinantný ľudský rastový faktor podobný inzulínu viažuci proteín 3'	Liečba leprechaunizmu
Slovenian	Rekombinantni človeški, inzulinu podobni rastni faktor-I/ protein, ki se veže na rekombinantni človeški, inzulinu podobni rastni faktor-3	Zdravljenje leprakonizma
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 leprechaunismo
Swedish	Recombinant human insulin-lik tillväxtfaktor I/ recombinant human insulin-lik tillväxtfaktor bindingsprotein-3	Behandling av leprechaunism
Norwegian	Rekombinant human insulinlignende vekstfaktor-I / protein-3' som binder rekombinant human insulinlignende vekstfaktor	Behandling av leprechaunisme
Icelandic	Raðbrigða insúlínlíkur vaxtarþáttur-I úr mönnum / prótein-3 sem bindur raðbrigða insúlínlíkan vaxtarþátt úr mönnum	Meðferð á Leprechaunismus