



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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EMA/COMP/77791/2004 Rev.1  
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 Rabson Mendnhall syndrome

*Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in March 2007 on request of the sponsor.*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/3/04/237) was granted by the European Commission to Insmmed 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 the Rabson Mendenhall syndrome.

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

### What is Rabson Mendehall syndrome?

Rabson Mendehall syndrome is an inherited condition characterized by extreme insulin resistance. 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. In this disease insulin is not able to function properly because insulin receptors have a defect. Symptoms of the Rabson-Mendenhall syndrome also include abnormalities of the head and face, abnormalities of the teeth and nails, and skin abnormalities such as acanthosis nigricans, a skin disorder characterized by abnormally increased coloration and velvety thickening (hyperkeratosis).

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

At the time of designation, Rabson Mendenhall syndrome 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 920 people, and is below

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\*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 Liechtenstein. This represents a population of 459,700,000 (Eurostat 2004).



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?**

No satisfactory methods exist that were authorised at the time of application for the treatment of Rabson Mendenhall syndrome. Treatments such as high fibre diet, and substances such as guar gum, and oral antidiabetics (e.g tolbutamide) or insulin were used. Treatment consisting of surgically removing the pituitary gland, and administering a substance called growth hormone were used in the most severe cases.

### **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 the defects in the insulin receptor or insulin signalling pathway that are present in patients with Rabson Mendnhall syndrome.

### **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 the Rabson Mendenhall syndrome 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.

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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<sup>1</sup>, 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 Rabson-Mendenhall syndrome
Czech	Rekombinantní lidský růstový faktor-I podobný inzulinu/ rekombinantní lidský růstový faktor vážící protein-3' podobný inzulinu	Léčba Rabson-Mendenhallova syndromu
Danish	Recombinant human insulin - ligende vækst faktor - I recombinant human insulin - ligende vækst faktor bindende protein -3	Behandling af Rabson-Mendenhall-syndrom
Dutch	Recombinant humaan insuline-achtige groei factor-I/recombinant humaan insuline-achtige groeifactor bindend proteïne-3	Behandeling van Rabson-Mendenhall-syndroom
Estonian	Rekombinantne inimese insuliinitaoline kasvufaktor-1 / rekombinantne inimese insuliinitaolist kasvufaktorit siduv valk-3	Rabson-Mendenhalli sündroomi ravi
Finnish	Rekombinantin ihmis-insuliinin kaltainen kasvutekijä-I/rekombinantti ihmis-insuliinin kaltainen kasvutekijää sitova proteiini-3	Rabson-Mendenhallin oireyhtymän hoito
French	Facteur de croissance insulino-mimétique recombinant de type I / Facteur de croissance insulino-mimétique recombinant lié à la protéine 3	Traitement du syndrome de Rabson-Mendenhall
German	Rekombinantes humanes Insulin-wie Wachstumsfaktor -I/rekombinantes humanes Insulin-wie Wachstumsfaktor, der protein-3 bindet	Behandlung von Rabson-Mendenhall-Syndrom
Greek	Ανασυνδουαζόμενος ανθρώπινος αυξητικός παράγοντας ομοιάζων με ινσουλίνη /ανασυνδουαζόμενη δέσμευτική πρωτεΐνη 3 του ανθρώπινου αυξητικού παράγοντα ομοιάζοντος με ινσουλίνη	Θεραπεία του συνδρόμου Rabson-Mendenhall
Hungarian	Rekombináns humán inzulinszerű növekedési fak-tor-I/rekombináns humán inzulinszerű növekedési faktort kötő fehérje-3	Rabson-Mendenhall szindróma kezelése
Italian	Fattore di crescita ricombinante umano insulino-simile I/ proteina ricombinante umana legante il fattore di crescita insulino-simile 3	Trattamento della sindrome di Rabson-Mendenhall
Latvian	Rekombinantais cilvēka insulīnam līdzīgais augšanas faktors-i/rekombinanto cilvēka insulīnam līdzīgo augšanas faktoru saistošais proteīns-3	Rebsona-Mendenhola sindroma ārstēšana

<sup>1</sup> 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	Rabson-Mendenhall sindromo gydymas
Maltese	Recombinant human insulin-like growth factor-I / recombinant human insulin-like growth factor binding protein-3	Treatment of Rabson-Mendenhall syndrome
Polish	Rekombinowany ludzki-insulinopodobny czynnik-wzrostu-I / białko-3' wiążące rekombinowany ludzki insulinopodobny czynnik-wzrostu	Leczenie zespołu Rabsona-Mendenhalla
Portuguese	Factor de crescimento análogo à insulina – I humano recombinante/proteína ligante do factor de crescimento análogo à insulina – 3 humana recombinante	Tratamento do síndrome de Rabson-Mendenhall
Slovak	Rekombinantný ľudský rastový faktor podobný inzulínu I / rekombinantný ľudský rastový faktor podobný inzulínu viažuci proteín 3'	Liečba Rabsonov-Mendehallovho syndrómu
Slovenian	Rekombinantni človeški, inzulinu podobni rastni faktor-I/ protein, ki se veže na rekombinantni človeški, inzulinu podobni rastni faktor-3	Zdravljenje Rabson-Mendehallovega sindroma
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 de Rabson-Mendenhall
Swedish	Recombinant human insulin-lik tillväxtfaktor I/ recombinant human insulin-lik tillväxtfaktor bindingsprotein-3	Behandling av Rabson-Mendehalls syndrom
Norwegian	Rekombinant human insulinlignende vekstfaktor-I / protein-3' som binder rekombinant human insulinlignende vekstfaktor	Behandling av Rabson-Mendehall-syndrom
Icelandic	Raðbrigða insúlínlíkur vaxtarþáttur-I úr mönnum / prótein-3 sem bindur raðbrigða insúlínlíkan vaxtarþátt úr mönnum	Meðferð við Rabson-Mendehall-heilkenni