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EMA/COMP/1338/2003 Rev.3
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 primary growth hormone insensitivity syndrome (Laron 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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in May 2007 on request of the sponsor.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 9 July 2003, orphan designation (EU/3/03/159) was granted by the European Commission to Dr. Geoffrey Allan, United Kingdom, for recombinant human insulin-like growth factor-I / recombinant human insulin-like growth factor binding protein-3 for the treatment of primary growth hormone insensitivity syndrome (Laron Syndrome).

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

What is primary growth hormone insensitivity syndrome (Laron Syndrome)?

Laron Syndrome is a growth disorder. The growth hormone (GH) is a natural hormone secreted in the body and responsible for the maturation and growth of the human body. In order to activate the cascade of molecular reactions which induce the biological activity of growth, the GH needs to bind to specific structures on the surface of cells: the GH receptors. Sometimes these GH receptors are defective and unable to respond to GH, in other words, the receptor is "insensitive" to the hormone, which is the case in patients with Laron syndrome. The reason why these receptor defects occur is unknown. Other mechanisms induced by the link of the GH to its receptor can be defective in Laron syndrome patients, such as insulin-like growth factor (IGF-I) production. IGF-I is actually the factor that stimulates body growth. Once the active insulin-like growth factor-I is released in the blood, it is bound to specific transport proteins, such as insulin-like growth factor binding protein 3 (IGFBP-3) in order to transport IGF-I to the tissues and in fact stimulate body growth. Primary growth hormone insensitivity syndrome (Laron syndrome) is a serious chronically debilitating condition.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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

At the time of designation, primary growth hormone insensitivity syndrome (Laron syndrome) affected approximately 0.03 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 1,100 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).

What treatments are available?

There were no approved treatments available for Laron syndrome at the time the application was made. However, insulin-like growth factor-I has been used for chronic treatments in patients affected by the condition.

How is this medicine expected to work?

The administration of insulin-like growth factor-I is expected to replace the missing active form of growth factor and thereby could produce similar effects on growth and differentiation. In addition, the administration of the complex of the active growth hormone together with its main transport protein (IGF-I/IGFBP-3) could have some advantages over the administration of IGF-I alone (e.g. increase of the mean time insulin growth factor-I is present in the blood, possible administration of higher doses of IGF-I).

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, no clinical trials in patients with primary growth hormone insensitivity syndrome (Laron syndrome) were initiated.

Recombinant human insulin-like growth factor-I / recombinant human insulin-like growth factor binding protein-3 was not marketed anywhere worldwide for the treatment of primary growth hormone insensitivity syndrome (Laron Syndrome), at the time of submission.

Orphan designation of recombinant human insulin-like growth factor-I / recombinant human insulin-like growth factor binding protein-3 was granted in the United States for treatment of growth hormone insensitivity syndrome and treatment of major burns that require hospitalisation.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 June 2003 recommending the granting of this designation.

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[*]Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001) and may differ from the true number of patients affected by the condition. This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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:

Insmed Europe Ltd
Compass House
Vision Park
Chivers Way
Histon
Cambridge CB4 9AD
United Kingdom
Telephone: + 44 1223 257 743
Telefax: + 44 1223 257 800
E-mail: information@insmed.com

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 primary growth hormone insensitivity syndrome (Laron Syndrome)
Czech	Rekombinantní lidský růstový faktor-I podobný inzulinu/ rekombinantní lidský růstový faktor vážící protein-3' podobný inzulínu	Léčba syndromu primární necitlivosti k růstovému hormonu (Laronův syndrom)
Danish	Recombinant human insulin - ligende vækst faktor - JEG recombinant human insulin - ligende vækst faktor indbinding protein -3	Behandling af primær væksthormon insensitivitetssyndrom (Laron Syndrome)
Dutch	Recombinant humane insuline-achtige groei factor-I/recombinant humane insuline-achtige groeifactor bindend proteïne –3	Behandeling van primair groeihormoon insensitiviteitssyndroom (Laron Syndroom)
Estonian	Rekombinantne inimese insuliinitaoline kasvufaktor-1 /rekombinantne inimese insuliinitaolist kasvufaktorit siduv valk-3	Primaarse kasvuhormooni insensitiivsuse sündroomi (Laron sündroomi) ravi.
Finnish	Rekombinantin ihmis-insuliinin kaltainen kasvutekijä–I/rekombinantti ihmis-insuliinin kaltainen kasvutekijää sitova proteiini-3	Primaarisen kasvuhormoni-insensitiivisyyssyndrooman hoito (Laron syndrooma)
French	Facteur de croissance insulinomimétique recombinant de type I / Facteur de croissance insulinomimétique recombinant lié à la protéine 3	Traitement du syndrome primaire de l'insensibilité à l'hormone de croissance (syndrome de Laron)
German	Recombinant Mensch Insulin-wie Mensch des Wachstums factor-I/recombinant Insulin-wie der Wachstumfaktor, der protein-3 bindet	Behandlung des primaeren Wachstumshormnon-insensitivitaetssyndroms (Laron Syndroms)
Greek	Ανασυνδυαζόμενος ανθρώπινος αυξητικός παράγοντας ομοιάζων με ινσουλίνη /ανασυνδυαζόμενη δέσμευτική πρωτεϊνη 3 του ανθρώπινου αυξητικού παράγοντα ομοιάζοντος με ινσουλίνη	Αγωγή κατά του συνδρόμου πρωτοπαθούς έλλειψης ευαισθησίας στην αυξητική ορμόνη (σύνδρομο Laron)

[1] At the time of transfer of sponsorship

Language	Active ingredient	Indication
Hungarian	Rekombináns humán inzulinszerű növekedési faktor-I/rekombináns humán inzulinszerű növekedési faktort kötő fehérje-3	Primer növekedési hormon érzéketlenségi szindróma (Laron syndroma)
Italian	Fattore di crescita ricombinante umano insulino-simile I/ proteina 3 ricombinante umana legante il fattore di crescita insulino-simile 3	Trattamento della sindrome da resistenza primaria all'ormone della crescita (sindrome di Laron)
Latvian	Rekombinantais cilvēka insulīnam līdzīgais augšanas faktors-i/rekombinanto cilvēka insulīnam līdzīgo augšanas faktoru saistošais proteīns-3	Primāra augšanas hormona nejūtības sindroms (laron sindroms)
Lithuanian	Rekombinantinis į žmogaus insuliną panašus augimo faktorius - I/rekombinantinis į žmogaus insuliną panašus augimo faktorius, susijungęs su baltymu-3	Pirminio nejautrumo augimo hormonui sindromo gydymas (Larono sindromas)
Polish	Rekombinowany ludzki insulinopodobny czynnika wzrostu-I /białko-3' wiążące rekombinowany ludzki insulinopodobny czynnika wzrostu	Leczenie pierwotnego zespołu niewrażliwości na czynnik wzrostu (zespół Laron'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 síndroma de insensibilidade primária à hormona do crescimento (Síndroma de Laron)
Slovak	Rekombinantný ľudský rastový faktor podobný inzulínu I / rekombinantný ľudský rastový faktor podobný inzulínu viažuci proteín 3'	Liečba primárneho syndrómu necitlivosti na rastový hormón (Laronov syndróm)
Slovenian	Rekombinantni človeški, inzulinu podobni rastni faktor-I/protein, ki se veže na rekombinantni človeški, inzulinu podobni rastni faktor-3	Zdravljenje primarne neodzivnosti na rastni hormon (Laronov sindrom)
Spanish	Factor de crecimiento-I similar a la insulina recombinante humano / proteína de unión al factor de crecimiento similar a la insulina-3 recombinante humana	Tratamiento del síndrome de resistencia primaria a la hormona de creciciento (Síndrome de Laron)
Swedish	Recombinant human insulin-lik tillväxtfaktor I/ recombinant human insulin-lik tillväxtfaktor bindingsprotein-3	Behandling av primärt tillväxthormoninsensitivitetssyndrom (Laron syndrom)