European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of mecasermin for the treatment of primary insulin-like growth factor-1 deficiency due to molecular or genetic defects

On 22 May 2006, orphan designation (EU/3/06/373) was granted by the European Commission to Tercica Europe Limited, Ireland, for mecasermin for the treatment of primary insulin-like growth factor-1 deficiency due to molecular or genetic defects.
The sponsorship was transferred to Tercica Europe Limited, Ireland, in December 2005 and subsequently to Ipsen Pharma, France, in July 2009.

What is primary insulin-like growth factor-1 deficiency due to molecular or genetic defects?
Insulin-like growth factor-1 (IGF-1) is a naturally occurring hormone secreted (produced) in the body which, together with growth hormone (GH), plays a central role in stimulating growth of the human body. Deficiency of IGF-1 results in short stature (height) and can be caused by an underlying molecular or genetic defect. There may be molecular defects in the specific structures on the surface of cells (receptors) that GH binds to, resulting in resistance to GH, or signalling defects in the cascade of molecular reactions which induce (stimulate) the biological activity of growth, or defects in expression of the gene that codes for production of IGF-1. In these cases the primary deficiency is circulating IGF-1, with GH levels being normal or elevated. The reason why these molecular or genetic defects occur is unknown.
Primary insulin-like growth factor-1 deficiency due to molecular or genetic defects is a serious and chronically debilitating condition.

What is the estimated number of patients affected by the condition?
At the time of designation primary insulin-like growth factor-1 deficiency due to molecular or genetic defects affected less than 2 in 10,000 people in the European Union (EU) [*]. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around 90,000 people.

What treatments are available?
There were no approved treatments for primary insulin-like growth factor-1 deficiency at the time of designation.

[*] 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).

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How is this medicine expected to work?
Mecasermin is a recombinant (artificially synthesised) human insulin-like growth factor-1. Once administered in patients with primary IGF-1 deficiency, mecasermin is expected to replace the natural IGF-1 in the body, thus compensating for its loss. Thus, mecasermin is expected to stimulate the growth of the body in the same way as IGF-1.

What is the stage of development of this medicine?
The effects of mecasermin were evaluated in experimental models. At the time of submission of the application for orphan designation, clinical trials in patients with primary insulin-like growth factor-1 deficiency were ongoing.

Mecasermin was authorised as an orphan medicinal product in the USA for 'the long-term treatment of growth failure in children with severe primary IGF-1 deficiency (Primary IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to growth hormone', 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 5 April 2006 a positive opinion recommending the grant of the above-mentioned designation.

Update: Mecasermin (Increlex) has been authorised in the EU since 3 August 2007 for the long-term treatment of growth failure in children and adolescents with severe primary insulinlike growth factor-1 deficiency (Primary IGFD).

Severe Primary IGFD is defined by:
• height standard deviation score ≤ –3.0 and
• basal IGF-1 levels below the 2.5th percentile for age and gender and GH sufficiency.
• Exclusion of secondary forms of IGF-1 deficiency, such as malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids.

Severe Primary IGFD includes patients with mutations in the GH receptor (GHR), post-GHR signaling pathway, and IGF-1 gene defects; they are not GH deficient, and therefore, they cannot be expected to respond adequately to exogenous GH treatment. It is recommended to confirm the diagnosis by conducting an IGF-1 generation test.

For more information on Increlex, see:
www.emea.europa.eu/humandocs/Humans/EPAR/increlex/increlex.htm

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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;
- and either the rarity of the condition (affecting not more than five in 10,000 people in the Community) or the 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 the quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

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Translations of the active ingredient and indication in all EU languages and Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Mecasermin	Treatment of primary insulin-like growth factor-1 deficiency due to molecular or genetic defects
Czech	Mecasermin	Léčba primárního deficitu inzulinu podobného růstového faktoru 1 (primární IGFD) v způsobeného molekulárním nebo genetickým defektem
Danish	Mecasermin	Behandling af primær insulinlignende vækstfaktor 1-mangel på grund af molekylære eller genetiske defekter
Dutch	Mecasermin	Behandeling van primaire insuline-achtige groeifactor-1 deficiëntie te wijten aan moleculaire of genetische defecten
Estonian	Mekasermiin	Molekulaarsetest või geneetilistest defektidest tingitud rimaarse insuliinisarnase kasvufaktori 1 puudulikkuse ravi
Finnish	Mekasermiini	Molekyyli- tai geenivirheestä johtuvan primaarin insuliininkaltaisen kasvutekijä 1:n puutoksen hoito
French	Mécasermine	Traitement de la carence primaire en facteur de croissance 1 analogue de l'insuline; d'origine moléculaire ou génétique
German	Mecasermin	Behandlung von primärem Mangel an insulin-ähnlichem Wachstumsfaktor 1 (primärer IGF-Mangel) verursacht durch molekulare oder genetische Defekte
Greek	Μηκασερμίνη	Θεραπευτική αγωγή της καθυστέρησης ανάπτυξης σε παιδιά με πρωτογενή ανεπάρκεια ινσουλινόμορφου αυξητικού παράγοντα-1 οφειλόμενη σε μοριακά ή γενετικά ελαττώματα
Hungarian	Mecasermin	Molekuláris vagy genetikai elváltozás okozta primer inzulin-szerű növekedési faktor-1 hiány kezelése
Italian	Mecasermina	Trattamento dell' insufficienza primaria nel fattore di crescita 1 tipo insulina d'origine molecolare o genetica
Latvian	Mekasermins	Molekulāru vai ģenētisku defektu izraisītas primāras insulīnam līdzīgā augšanas faktora-1 nepietiekamības ārstēšana
Lithuanian	Mekaserminas	Pirminio į insuliną panašaus augimo faktoriaus 1 stokos gydymas dėl molekulinio ar genetinio defekto
Polish	Mecasermin	Leczenie pierwotnego niedoboru insulinopodobnego czynnika-1 wzrostu, spowodowanego uszkodzeniem genetycznym lub cząsteczkowym
Portuguese	Mecasermina	Tratamento da deficiência primária em factor de crescimento de tipo insulínico 1 causada por factores genéticos ou moleculares
Slovak	Mecasermin	Liečba primárneho nedostatku inzulínu podobného rastového faktora 1 spôsobená molekulárnou alebo genetickou poruchou
Slovenian	Mekasermin	Zdravljenje pomanjkanja insulinu podobnega rastnega faktorja-1 zaradi molekularnega ali genetskega defekta
Spanish	Mecasermina	Tratamiento de la deficiencia primaria de factor de crecimiento insulínico de tipo 1 debido a defectos moleculares o genéticos
Swedish	Mekasermin	Behandling av primär insulinliknande tillväxtfaktor-1 brist beroende pa mollekylära eller genetiska defekt
Norwegian	Mecasermin	Behandling av insulinlignende vekstfaktor-1 mangel pga molekylær eller genetisk defekt
Icelandic	Mecasermín	Meðferð við frumkomnum skorti á insúlín-líkum vaxtarþætti-1 sem stafar af mólekúlar- eða erfðagalla