



Press release

Increlex[®] receives marketing authorisation in the European Union

Increlex[®] is the first recombinant human insulin-like growth factor-1 therapy approved in Europe for severe primary IGF-1 deficiency

Paris (France), 9 August 2007 - Ipsen (Euronext: FR0010259150; IPN) today announced that the European Commission granted marketing authorisation for Increlex[®] (mecasermin) 10 mg/ml solution for injection in the European Union.

The indication approved is for the long-term treatment of growth failure in children and adolescents with severe primary insulin-like growth factor-1 deficiency (severe primary IGFD).

Increlex[®] was designated as an orphan medicinal product in the European Union on 22 May 2006. The European marketing authorisation provides Increlex[®] a ten-year marketing exclusivity for the treatment of severe Primary IGFD.

In October 2006, Tercica Inc. granted Ipsen the development and commercialisation rights for Increlex[®] in Europe and certain other territories; Ipsen is now in the process of launching this drug from October 2007 in the European Union. According to the terms of the agreement, the approval of Increlex[®] marketing authorisation in the European Union triggers a €15 million (approximately US\$20 million) milestone payment by Ipsen to Tercica.

“The effect of growth hormone (GH) is to a major part mediated by insulin-like growth-factor-1 (IGF-1). If the biochemical steps leading to the formation of IGF-1 are interrupted then patients are suffering from primary IGF-1 deficiency and cannot respond to GH therapy. Replacement with IGF-1 is the pathogenetically appropriate therapy in these instances” said Professor Dr. Michael B. Ranke, Paediatric Endocrinology Section, University Children's Hospital, University of Tuebingen, Germany. *“Increlex[®] (mecasermin), a recombinant human insulin-like growth factor-1 (IGF-1) thus opens a new field for the treatment of previously untreatable children with severely short stature.”*

Christophe Jean, Executive Vice-President and Chief Operating Officer of Ipsen, and Board member of Tercica Inc., said “We are very pleased that Increlex[®] will be soon available to patients and physicians for the treatment of growth failure in children and adolescents with severe primary IGF-1 deficiency. Increlex[®] fits perfectly in our existing global endocrinology franchise, along with Somatuline[®] and NutropinAq[®] to provide endocrinologists with a comprehensive solution for the treatment of patients suffering from growth disorders.”

About the marketing authorisation

(The European Public Assessment Report (EPAR) summary can be accessed at <http://www.emea.europa.eu>)

This decision follows the filing by Tercica Inc., Ipsen's partner, of an application for marketing authorisation for Increlex[®] in the European Union in December 2005. The positive opinion, recommending to grant a marketing authorisation under exceptional circumstances for Increlex[®], was adopted by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) on 24 May 2007. Such authorisations are permissible for medicinal products for which the applicant can demonstrate that comprehensive data cannot be provided, for example because of the rarity of the condition, as long as it can be demonstrated on a regular basis that the benefits outweigh the risks. Every year, Ipsen and Tercica will review with the EMA any new information that may become available.

The positive decision of the EMA is based on clinical data from 76 patients who were treated with Increlex[®] for up to 12.5 years. The primary endpoint in the pivotal clinical study was height velocity, which increased from an average of 2.8 cm per year at baseline to an average of 8.0 cm per year ($p < 0.0001$) in the first year of treatment and 5.8 cm in the second. The growth rate stabilised at around 4.7 cm per year from the fourth year of treatment.

About Increlex[®]

Mechanism of action

The active ingredient of Increlex[®] is recombinant human insulin-like growth factor-1 (IGF-1). IGF-1 is the direct mediator of growth hormone's effect on statural growth, and must be present for normal growth of bones and cartilage in children. In severe primary IGFD, children's serum IGF-1 levels are low, despite the presence of normal or elevated GH level. Without adequate IGF-1, children cannot achieve normal height. In children with this disorder, low IGF-1 levels are due to growth hormone resistance associated with mutations in GH receptors, post-GH receptor signalling pathways, or to defects in IGF-1 gene expression. As such, these children cannot be expected to respond adequately to exogenous GH treatment. Some individuals may also have a range of metabolic disorders, including lipid abnormalities, decreased bone density, obesity and insulin resistance.

Indication

The summary of product characteristics defines severe Primary IGFD as:

- a height standard deviation score ≤ -3.0 ,
- basal IGF-1 levels below the 2.5th percentile for age and gender,
- GH sufficiency, and
- the exclusion of secondary forms of IGF-1 deficiency, such as malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids.

It is recommended to confirm the diagnosis by conducting an IGF-1 generation test.

Doses

The recommended starting dose is 0.04 mg per kilogram body weight twice a day. The dose should be tailored for each patient according to the speed of growth and certain side effects. The maximum dose is 0.12 mg per kilogram twice a day.

Increlex[®] is given by injection under the skin, and the injection site should be changed with each injection. The injection should be carried out shortly before or after a meal or snack.



Safety information

The most common side effects with Increlex[®] (seen in more than 1 patient in 10) are hypoglycaemia (low blood sugar levels), thymus hypertrophy (growth of the thymus gland, a gland below the breastbone that is involved in producing infection-fighting cells), headache, hypoacusis (hearing loss), tonsillar hypertrophy (growth of the tonsils), snoring and injection site hypertrophy (lumps at the site of injection). For the full list of all side effects reported with Increlex[®], see the Summary of Product Characteristics.

Increlex[®] should not be used in people who may be hypersensitive (allergic) to mecasecimerin or any of the other ingredients. It should also not be used in patients who have, or are thought to have active neoplasia (abnormal cell growth). Treatment with Increlex[®] should be stopped if neoplasia develops. It should not be used in babies.

Marketing

Increlex[®] has been marketed in the United States by Tercica, Inc. since early 2006.

Note to editors

The regulatory status of medications as referred to in these materials may vary from country to country. Please refer to the local product label and prescribing information.

About Ipsen

Ipsen is an innovation driven international specialty pharmaceutical group with over 20 products on the market and a total worldwide staff of nearly 4,000. The company's development strategy is based on a combination of products in targeted therapeutic areas (oncology, endocrinology and neuromuscular disorders) which are growth drivers, and primary care products which contribute significantly to its research financing. This strategy is also supported by an active policy of partnerships. The location of its four Research and Development centres (Paris, Boston, Barcelona, London) gives the Group a competitive edge in gaining access to leading university research teams and highly qualified personnel. In 2006, R&D expenditure was €178.3 million, i.e. 20.7% of consolidated sales, which amounted to €861.7 million while total revenues amounted to €945.3 million (in IFRS). 700 people in R&D are dedicated to the discovery and development of innovative drugs for patient care. Ipsen's shares are traded on Segment A of Eurolist by EuronextTM (stock code: IPN, ISIN code: FR0010259150). Ipsen's shares are eligible to the "Système à Règlement Différé" ("SRD") and the Group is part of the SBF 250 index. For more information on Ipsen, visit our website at www.ipсен.com.

Forward-looking statements

The forward-looking statements and targets contained herein are based on Ipsen's management's current views and assumptions. Such statements involve known and unknown risks and uncertainties that may cause actual results, performance or events to differ materially from those anticipated herein. Moreover, the Research and Development process involves several stages at each of which there is a substantial risk that the Group will fail to achieve its objectives and be forced to abandon its efforts in respect of a product in which it has invested significant sums. Therefore, the Group cannot be certain that favourable results obtained during pre-clinical trials will be confirmed subsequently during clinical trials, or that the results of clinical trials will be sufficient to demonstrate the safe and effective nature of the product concerned. Ipsen expressly disclaims any obligation or undertaking to update or revise any forward looking statements, targets or estimates contained in this press release to reflect any change in events, conditions, assumptions or circumstances on which any such statements are based, unless so required by applicable law. Ipsen's business is subject to the risk factors outlined in its information documents filed with the French *Autorité des Marchés Financiers*.

**About Tercica**

Tercica is a biopharmaceutical company committed to improving endocrine health by partnering with the endocrine community to develop and commercialize new therapeutics for pediatric and adult growth disorders, and for adult metabolic disorders. For further information on Tercica, please visit www.tercica.com.

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