

**IMPORTANT SUPPLY
INTERRUPTION INFORMATION**

April 25, 2013

Dear Dr. **[Insert doctor's name.]**

As a valued partner in short stature patient care, I am writing today to notify you of an interruption to the supply of Increlex[®] (mecasermin, rhIGF-1). Due to operational problems at our third party manufacturer, supply is now limited and will be completely exhausted in the near future. Ipsen is working closely with its suppliers and the U.S. Food and Drug Administration (FDA) to manage the shortage period and to expedite an orderly reinstatement of normal Increlex[®] supply arrangements.

At present levels of demand, we anticipate our ability to meet Increlex[®] order requests will stop at the beginning of June 2013; we are unable to tell you at the present time for how long this interruption of supply will last. However, in view of this imminent shortage, we recommend that new patients are not started on Increlex[®] therapy until normal supplies are reestablished. As ever, clinical decisions such as these must be left to you as the treating physician in the best interest of your patients.

Ipsen is not aware of any other approved IGF-1 pharmaceutical product in the European Union/USA. There are only limited data on the clinical consequences of stopping Increlex[®] treatment in patients with Severe Primary IGF-1 Deficiency.^{1,2} Ipsen cannot provide medical management advice for individual patients.

As a company focused on patient care, we understand this supply interruption impacts patients, their families and the endocrinology community. We are working as quickly as possible to address this issue with our suppliers and the FDA to reinstate normal supplies of Increlex[®] as soon as possible. We will write to you as soon as the re-supply timelines become clearer.

Should you have questions concerning the information in this letter, please contact us directly by phone at 855-463-5127 or by email at druginfo@medcomsol.com.

Indication

Increlex[®] (mecasermin [rDNA origin] injection) is indicated for the treatment of growth failure in children with severe primary IGF-1 deficiency, or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH. Severe primary IGF-1 deficiency (IGFD) is defined by height standard deviation score ≤ -3.0 and basal IGF-1 standard deviation score ≤ -3.0 and normal or elevated growth hormone (GH).

Increlex is not intended for use in subjects with secondary forms of IGF-1 deficiency, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids. Thyroid and nutritional deficiencies should be corrected before initiating Increlex treatment.

Limitations of use: Increlex is not a substitute to GH for approved GH indications.

Increlex has not been studied in children < 2 years of age.

Important Safety Information**Contraindications:**

- Presence of active or suspected malignancy
- Hypersensitivity to mecasermin (rhIGF-1) or any of the inactive ingredients in Increlex
- Intravenous administration
- Closed epiphyses

Please see additional Important Safety Information on the next page and accompanying full Prescribing Information.

Important Safety Information (continued from page 1)

Warnings and Precautions:

- Hypoglycemic Effects: Increlex should be administered 20 minutes before or after a meal or snack, and should not be administered when the meal or snack is omitted.
- Hypersensitivity: Allergic reactions have been reported, including anaphylaxis requiring hospitalization.
- Intracranial hypertension: Fundoscopic examination is recommended at the initiation of and periodically during the course of therapy.
- Tonsillar/adenoidal hypertrophy: Patients should have periodic examinations to rule out potential complications.
- Slipped capital femoral epiphysis: Evaluate any child with onset of limp or hip/knee pain.
- Progression of scoliosis: Monitor any child with scoliosis.

Common adverse reactions include: hypoglycemia, local and systemic hypersensitivity, and tonsillar hypertrophy.

You are encouraged to report suspected adverse events to Ipsen at 855-463-5127 or directly to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch/report.htm.

Thank you for being our partners in treating and caring for patients.

Sincerely,

Sean McKercher
President & General Manager
Ipsen Biopharmaceuticals, Inc.

¹ Concolino et al. Long-term treatment with recombinant insulin-like growth factor 1 (IGF-1) in a child with IGF-1 gene mutation. *Eur J Pediatr*, 2010, 169:245-7

² Besson A et al. Primary GH insensitivity (Laron Syndrome) caused by a novel 4kb deletion encompassing exon 5 of the GH receptor gene: effect of intermittent long-term treatment with recombinant human IGF-1. *Eur J Endocrinology*, 2004, 150:635-42