



March 2013

IMPORTANT SAFETY INFORMATION REGARDING
INCRELEX® (mecasermin [rhiGF origin] injection)

Dear Healthcare Professional,

Ipsen Biopharmaceuticals, Inc. (Ipsen) is currently coordinating with the Food and Drug Administration (FDA) to release supply of Increlex® (mecasermin [rDNA origin] injection) manufactured by Ipsen's third party supplier using an alternative drug substance manufacturing facility that has not been approved by the FDA. In an effort to address a potential shortage situation for Increlex®, the U.S. Food and Drug Administration (FDA) exercised its regulatory discretion for Increlex® Lots #081603F and #121353F, manufactured using drug substance supplied by such new manufacturing facility which is not yet approved by FDA. These Increlex® lots contain drug substance supplied by this new manufacturing facility and have undergone a full Ipsen internal review to ensure that they meet quality and safety standards. Ipsen will continue to work with its third party supplier and with the FDA to seek approval for the supplier's new drug substance manufacturing facility for the production of increlex® to minimize any potential supply disruptions. Increlex® is indicated for the treatment of growth failure in children with severe Primary IGF1D."

Patient safety is a primary concern at Ipsen and we continue to encourage you to report any adverse event experienced by your patients treated with INCRELEX® that you consider may be related to treatment.

Examples of potential adverse events include the following:

- Hypersensitivity
- Increased immunogenicity
- Loss of efficacy
- Reduction in pharmacologic activity
- Injection site reactions

In our continuing efforts to monitor the safety and efficacy of INCRELEX®, your attention to reporting treatment-related adverse events in general and specifically in the five categories bulleted above, is requested. Suspected adverse events may be reported to Ipsen at 1-866-837-2422 or directly to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch/report.htm

INCRELEX is contraindicated in the presence of active or suspected malignancy, and therapy should be discontinued if evidence of malignancy develops. INCRELEX should not be used by patients who are allergic to mecasermin (rhiGF-1) or any of the inactive ingredients in INCRELEX, or who have experienced a severe hypersensitivity to INCRELEX





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[see Warnings and Precautions and Adverse Reactions]. Intravenous administration of INCRELEX is contraindicated. INCRELEX should not be used for growth promotion in patients with closed epiphyses.

INCRELEX has insulin-like hypoglycemic effects and should be administered 20 minutes before or after a meal or snack. Hypersensitivity and allergic reactions have been reported,

including a low number of cases indicative of anaphylaxis requiring hospitalization. Intracranial hypertension has occurred in patients treated with INCRELEX. Funduscopic examination is recommended at the initiation of and periodically during the course of therapy. Patients should have periodic examinations to rule out potential complications from tonsillar/adenoidal hypertrophy and receive appropriate treatment if necessary. Children with onset of limp or hip/knee pain should be evaluated for possible slipped capital femoral epiphysis. Monitor any child with scoliosis for progression of the spine curve.

In clinical studies of 71 pediatric subjects with severe Primary IGF1 deficiency representing 274 patient-years of treatment, no subjects discontinued due to adverse events. Hypoglycemia was reported by 30 subjects (42%) at least once during their course of therapy with INCRELEX. Most cases of hypoglycemia were mild or moderate in severity. Five subjects had severe hypoglycemia (requiring assistance and treatment) on one or more occasion and four subjects experienced hypoglycemic seizures/loss of consciousness on one or more occasion. Symptomatic hypoglycemia was generally avoided when a meal or snack was consumed either shortly (i.e., 20 minutes) before or after the administration of INCRELEX. Tonsillar hypertrophy was noted in 11 (15%) subjects in the first 1 to 2 years of therapy with lesser tonsillar growth in subsequent years. Intracranial hypertension occurred in three subjects. In two subjects the events resolved without interruption of INCRELEX treatment. INCRELEX treatment was discontinued in the third subject and resumed later at a lower dose without recurrence.

Questions relating to Ipsen, INCRELEX® or this communication should be directed to wes.cetnarowski@ipsen.com or 1-908-275-6488.

Yours sincerely,

Wes Cetnarowski MD
VP, Chief Medical & Regulatory Affairs Officer N.A.

Enc: INCRELEX® U.S. Package Insert (Rev. September 2012)

INCRELEX® is a registered trademark of Ipsen Biopharmaceuticals, Inc.

