IPSEN
Innovation for patient care

Important Drug Information Update

Subject: Availability of INCRELEX® (mecasermin [rDNA origin] injection)

January 23, 2015

Dear Healthcare Professional,

In order to alleviate the current critical shortage of INCRELEX® (mecasermin [rDNA origin] injection), Ipsen Biopharmaceuticals, Inc. (Ipsen) is coordinating with the U.S. Food and Drug Administration (FDA) to increase the availability of the drug. At this time, FDA is not objecting to the release of INCRELEX Lot# 360953F, in an effort to address the current critical shortage of mecasermin [rDNA origin] injection. This lot was produced at an alternate manufacturing facility that has not been approved by the FDA.

Although the manufacturing facility has not been approved by the FDA, the additional lot of INCRELEX has undergone a full Ipsen internal review to ensure that it meets quality and safety standards. Ipsen's goal is to supply INCRELEX without interruption to the healthcare providers and patients who need it. Ipsen will continue to seek FDA approval of a new manufacturing site to ensure sufficient supply of INCRELEX for physicians and their patients as this remains a priority for Ipsen.

Upon physician request, Ipsen's support service, IPSEN CARES (Coverage, Access, Reimbursement & Education Support) can assist with initiating INCRELEX therapy for new and existing patients. Also upon physician request, IPSEN CARES can arrange for a nurse from the IPSEN CARES Nurse Network to retrain parents and caregivers on the appropriate injection technique for INCRELEX. Ipsen encourages families and caregivers to reach out to their healthcare professional with questions. Parents and caregivers can also call IPSEN CARES at 866-435-5677 with questions.

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 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. To report adverse events, product quality complaints, or to request medical information related to INCRELEX, please contact 855-463-5127.

Adverse events may also be reported to the FDA's MedWatch Adverse Event Reporting Program either online, or regular mail, or by fax:

- Online: www.fda.gov/medwatch/report.htm
- Regular mail: Use postage-paid FDA form 3500 available at www.fda.gov/MedWatch/getforms.htm.
  Mail to: MedWatch, FDA, 5600 Fishers Lane, Rockville, MD 20852-9787
- Telephone: 1-800-332-1088
- Fax: 1-800-FDA-0178

Yours sincerely,

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Indication and Important Safety Information

Indication

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

INCRELEX is not intended for use in subjects with secondary forms of IGFD, 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

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: Funduscopic 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.

Enc: INCRELEX® U.S. Prescribing Information (Rev. May 2014)