

Attachment #11



Important Safety Information

Contraindications

- Growth hormone should not be initiated to treat patients with acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma, or to patients having acute respiratory failure.
- Growth hormone should not be used for growth promotion in subjects with closed epiphyses or in patients with active neoplasia. Growth hormone should be discontinued if evidence of neoplasia develops.

Precautions

- Intracranial hypertension has been reported in a small number of patients treated with growth hormone. Funduscopic examination of patients is recommended at the initiation of and periodically during GH therapy. As with any protein, local or systemic allergic reactions may occur. Parents/patients should be advised to seek prompt medical attention if allergic reactions occur.
- GH may reduce insulin sensitivity, particularly in obese individuals; patients should be observed for evidence of glucose intolerance. For patients with diabetes mellitus, the insulin dose may require adjustment when GH therapy is instituted.
- Patients with symptomatic hypoglycemia associated with GHD should be closely monitored.
- Slipped capital femoral epiphysis may occur more frequently in patients with endocrine disorders or in patients undergoing rapid growth.
- Because GH increases growth rate, patients with a history of scoliosis who are treated with GH should be monitored for progression of scoliosis. GH has not been shown to increase the

incidence of scoliosis.

Adverse Reactions

Adverse reactions observed less frequently in clinical trials but were considered possibly, probably, or definitely related to Nutropin Depot therapy included headache (13% of subjects), nausea (8%), lower extremity pain (7%), fever (7%), and vomiting (5%). Please discuss with your physician first, then refer to the full prescribing information for the risks and benefits associated with growth hormone therapy.

Injection-Site Reactions

- Injection site reactions (ISRs) with Nutropin Depot occurred in nearly all patients and were generally mild to moderate and all resolved without intervention.
- In clinical studies involving 138 pediatric patients, Nutropin Depot demonstrated a safety profile similar to that of daily growth hormone therapy, with the exception of frequency and type of ISRs.
- The most frequent ISR was the occurrence of a pea-sized nodule formed by Nutropin Depot microspheres under the skin. Nodules gradually disappear as the microspheres degrade and the growth hormone is released.
- In Phase III trials, pain reported during injection decreased over time as patients gained experience with the therapy.
- Pain post-injection, often reported as tenderness or soreness to the touch, was also reported.

The most frequent adverse reactions associated with Nutropin Depot therapy were injection site-related, which occurred in nearly all patients. On average, 2 to 3 injection site-reactions were reported per injection, and included: nodules (61% of injections), erythema (53%), pain post-injection (47%), pain during injection (43%), bruising (20%), itching (13%), lipoatrophy (13%), and swelling or puffiness (8%). The intensity of these reactions was generally rated mild to moderate, with pain during injection occasionally rated as severe (7%), and all resolved without further intervention.

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