Sermorelin DESCRIPTION

Sermorelin acetate (sermorelin) is the acetate salt of an amidated synthetic 29- amino acid peptide (GRF 1-29 NH 2) that corresponds to the amino-terminal segment of the naturally occurring human growth hormone-releasing hormone (GHRH or GRF) consisting of 44 amino acid residues. The structural formula for sermorelin acetate is:

The free base of sermorelin has the empirical formula C 149 H 246 N 44 O 42 S and a molecular weight of 3,358 daltons.

Sermorelin is a sterile, non-pyrogenic, lyophilized powder intended for subcutaneous injection after reconstitution with Sodium Chloride Injection, USP. The reconstituted solution has a pH of 5.0 to 5.5.

Sermorelin is available in vials. The quantitative composition per vial is:

- 0.5 mg vial: Each vial contains 0.5 mg sermorelin (as the acetate) and 5 mg mannitol. The pH is adjusted with dibasic sodium phosphate and monobasic sodium phosphate buffer.
- 3.0 mg vial: Each vial contains 3.0 mg sermorelin (as the acetate) and 5 mg mannitol. The pH is adjusted with dibasic sodium phosphate and monobasic sodium phosphate buffer.

INDICATIONS

Sermorelin is approved for diagnostic evaluation of pituitary function and also for increasing growth in children. Off label usage may include acute or age-related growth hormone insufficiency.

DOSAGE AND ADMINISTRATION

A dosage of 0.2 - 0.3 mcg once daily at bedtime by subcutaneous injection is recommended. It is also recommended that subcutaneous injection sites be periodically rotated.

To prevent possible contamination, wipe the rubber vial stopper with an antiseptic solution before puncturing it with the needle. It is recommended that Sermorelin be administered using sterile, disposable syringes and needles. The syringes should be of small enough volume that the prescribed dose can be drawn from the vial with reasonable accuracy.

To reconstitute Sermorelin, inject the diluent into the vial of Sermorelin aiming the liquid against the glass vial wall. Swirl the vial with a GENTLE rotary motion until contents are dissolved completely. Do not administer Sermorelin if particles are visible in the reconstituted solution or if the reconstituted solution is cloudy.

HOW SUPPLIED

Vials of Sermorelin (sermorelin acetate for injection) should be stored refrigerated (2°-8°C/36°-46°F). Expiration dates are stated on the labels.

Sermorelin acetate (sermorelin) is a sterile, nonpyrogenic, lyophilized powder supplied in packages containing:

1 vial 0.5 mg Sermorelin and 1 vial 2 mL Sodium Chloride Injection

1 vial 3.0 mg Sermorelin and 1 vial 2 mL Sodium Chloride Injection

SIDE EFFECTS

A large proportion of patients develop anti- GRF antibodies at least once during treatment with Sermorelin. The significance of these antibodies is not clear and often a positive test at one growth assessment will become negative by the next assessment. The presence of antibodies does not appear to affect growth or appear to be related to a specific adverse reaction profile. No generalized allergic reactions to Sermorelin have been reported.

The most common treatment-related adverse event (occurring in about 1 patient in 6) is local injection reaction characterized by pain, swelling or redness. Of 350 patients exposed to Sermorelin in clinical trials, three discontinued therapy due to injection reactions. Other treatment-related adverse events had individual occurrence rates of less than 1% and include: headache, flushing, dysphagia, dizziness, hyperactivity, somnolence and urticaria.

When administered intravenously for diagnostic use, the following adverse reactions have been noted: flushing of the face, injection site pain, redness and/or swelling, nausea, headache, vomiting, dysgeusia, pallor and tightness in the chest.

Drug Abuse and Dependence

The clinical pharmacology suggests that Sermorelin is very unlikely to be associated with drug abuse or dependence and there have been no reports of this from clinical trials

Sermorelin INTERACTIONS

Concomitant glucocorticoid therapy may inhibit the response to Sermorelin.

WARNINGS

No information provided.

PRECAUTIONS

General: Sermorelin acetate therapy should be carried out under the regular guidance of a physician who is experienced in the diagnosis and management of growth hormone deficiencies.

In clinical studies, the incidence of hypothyroidism during Sermorelin therapy was 6.5%. In the largest clinical study, 8 of 110 enrolled patients were on thyroid replacement therapy prior to Sermorelin therapy and an additional 5 after initiating therapy. Untreated hypothyroidism can jeopardize the response to Sermorelin . Therefore, thyroid hormone determinations should be performed before the initiation and throughout the duration of Sermorelin therapy. Thyroid hormone replacement therapy should be initiated when indicated.

Patients with growth hormone deficiency secondary to an intracranial lesion were not studied in clinical trials. It is not recommended that such patients be treated with Sermorelin .

As with the administration of any peptide, local or systemic allergic reactions may occur. P atients should be informed that such reactions are possible and that prompt medical attention should be sought if allergic reactions occur.

Laboratory Tests: Serum levels of inorganic phosphorus, alkaline phosphatase, GH and IGF-1 may increase with Sermorelin therapy.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies for carcinogenicity and impairment of fertility have not been performed with Sermorelin . There has been no evidence from studies to date of Sermorelin -induced genetic toxicity.

Pregnancy: Pregnancy Category C. During teratology studies Sermorelin produced minor variations in fetuses of rats and rabbits when given at a dose of 0.5 mg/kg/day. This dose is approximately 3 and 6 times the daily human dose calculated on a body surface area (mg/m 2) basis, for rats and rabbits, respectively. There are no adequate and well controlled studies in pregnant women. Sermorelin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Women: It is not known whether Sermorelin is excreted in human milk. Because many drugs are excreted in human milk, cautions should be exercised when Sermorelin is administered to a nursing women.

OVERDOSE

The recommended dosage of Sermorelin (sermorelin acetate for injection) should not be exceeded.

CONTRAINDICATIONS

Sermorelin should not be used by patients with a known sensitivity to sermorelin or any of the excipients.

CLINICAL PHARMACOLOGY

Sermorelin acetate for injection increases plasma growth hormone (GH) concentration by stimulating the pituitary gland to release GH. Sermorelin is similar to the native hormone (GRF [1-44]-NH 2) in its ability to stimulate GH secretion in humans. Pharmacokinetics

Absorption

In subcutaneous administration of 2 mg sermorelin to 12 normal volunteers, peak concentrations of sermorelin were reached in 5-20 minutes. The mean absolute bioavailability after SC administration is about 6%.

Distribution

After intravenous administration of 0.25-1.0 mg Sermorelin® to 12 normal volunteers, the mean volume of distribution ranged between 23.7-25.8 liters.

Metabolism

No metabolism studies have been performed in humans.

Elimination

Sermorelin is rapidly cleared from the circulation, with clearance values in adults ranging between 2.4-2.8 L/min. The halflife of Sermorelin is short, 11-12 minutes after either intravenous or subcutaneous administration.

Special Populations

Gender/Age: No gender data are available in pediatric patients. In normal adults, the clearance of sermorelin in men and women is similar. No age data are available.

Renal/Hepatic Insufficiency: No data are available.

PATIENT INFORMATION

Patients being treated with Sermorelin and/or their parents should be informed of the potential benefits and risks associated with treatment. If home use is determined to be desirable by the physician, instructions on appropriate use should be given, including a review of the contents of the Patient Information Insert. This information is intended to aid in the safe and effective administration of the medication. It is not a disclosure of all possible adverse or intended effects.

If home use is prescribed, a puncture resistant container for the disposal of used syringes and needles should be recommended to the patient. Patients and/or parents should be thoroughly instructed in the importance of proper disposal and cautioned against any reuse of needles and syringes (see Patient Information Insert).