OCTREOTIDE ACETATE INJECTION

DESCRIPTION
OCTREOTIDE acetate injection, a cyclic somatostatin analogue as similar to the natural hormone somatostatin. It is an even more potent inhibitor of growth hormone, glucose, and insulin than somatostatin. As somatostatin, it also suppresses lipase and glucagon secretion, decreases insulin secretion and release from glucagonomas, gastrin, vasoactive intestinal polypeptide (VIP), substance P, motilin, and pancreatic polypeptide.

Acromegaly: Growth Hormone, IGF-I (somatomedin C) Responsiveness to octreotide acetate may be evaluated by determining growth hormone levels before and 1 hour after subcutaneous injection of the natural hormone somatostatin.

Acromegaly: somatostatin acetate, available as single 0.1 mL vial containing 100 mcg of the natural hormone somatostatin. Acromegaly: somatostatin acetate injection is available as single 0.1 mL vial containing 100 mcg of the natural hormone somatostatin.

OCTREOTIDE may restore fertility. Female patients of childbearing potential should be advised to use adequate contraception during treatment with OCTREOTIDE acetate injection.

Risk of Pregnancy with Normalization of IGF-1 and GH: OCTREOTIDE acetate injection is contraindicated in patients who are sensitive to this drug or any of its components. OCTREOTIDE acetate injection is contraindicated in patients who are sensitive to this drug or any of its components. OCTREOTIDE acetate injection is contraindicated in patients who are sensitive to this drug or any of its components. OCTREOTIDE acetate injection is contraindicated in patients who are sensitive to this drug or any of its components.

CONTRAINDICATIONS:
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Pharmacokinetics: After subcutaneous injection, octreotide acetate is absorbed rapidly and completely from the injection site. Peak concentrations of octreotide acetate are observed 1–3 hours after injection. Plasma concentrations peak 1–4 hours after subcutaneous injection. Octreotide acetate is eliminated primarily by renal excretion as unchanged drug (77% in 24 hours) and metabolites (13% in 24 hours). The terminal half-life of octreotide acetate is approximately 10 hours.

In healthy volunteers the distribution of octreotide acetate from plasma was rapid (0.4 to 0.6 hours), the volume of distribution was estimated to be 0.5 to 1.0 times the body weight, the clearance was approximately 140 mL/min per 1.73 m², and the body clearance was approximately 1.3 L/min.

In patients with acute peptic ulcer disease, the pharmacokinetics of octreotide acetate were not significantly different from those in healthy volunteers. A mean peak concentration of 24 ng/mL was observed 1 hour after subcutaneous injection. The volume of distribution of the bound drug was estimated to be 1.4 ± 0.3 L/kg, and the body distribution was increased in 1.8 to 2.5. The disposition of octreotide acetate was similar in fast and slow titrating subjects.

In patients with chronic peptic ulcer disease, the pharmacokinetics of octreotide acetate were not significantly different from those in healthy volunteers. The mean peak concentration of octreotide acetate was 24 ng/mL, the volume of distribution was approximately 0.5 L/kg, and the body distribution was increased in 1.8 to 2.5.

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In patients with chronic peptic ulcer disease, the pharmacokinetics of octreotide acetate were not significantly different from those in healthy volunteers. The mean peak concentration of octreotide acetate was 24 ng/mL, the volume of distribution was approximately 0.5 L/kg, and the body distribution was increased in 1.8 to 2.5.
Dialysis, total body clearance was reduced to about half that found in healthy subjects (from approximately 10 L/hr to 4.5 L/hr).

Type II diabetics with partially intact insulin reserves, octreotide acetate administration may result in decreases in plasma insulin levels.

Several cases of pancreatitis have been reported in patients receiving octreotide acetate therapy.


dosage may be initiated at 50 mcg t.i.d. Beginning with this low dose may permit adaptation to adverse gastrointestinal effects for patients who will require higher doses. IGF-I (somatomedin C) levels every 2 weeks can be used to guide titration. Alternatively, a single measurement of IGF-I (somatomedin C) level on the specific tumor. Based on diagnosis, measurement of the following substances may be useful in monitoring the progress of disease activity:

endocrine, gastrointestinal, cardiovascular, renal, hepatic, pulmonary, and CNS effects. The following adverse reactions have been identified during the postapproval use of octreotide acetate.

- Gastrointestinal:
  - Nausea
  - Vomiting
  - Diarrhea
  - Abdominal pain
  - Abdominal distention
  - Abdominal cramps
  - Bowel obstruction
  - Ascites

- Cardiac:
  - Sinus bradycardia (< 50 bpm) developed in 25%; conduction abnormalities occurred in 10% and arrhythmias in 4%.

- Hypoglycemia, hypoglycemia observed in 3% and 10% of patients, respectively, but only in 0.2% and 0.4% of patients, respectively.

- Hypertension was observed in 2% of patients.

- Other events (relationship to drug not established), each observed in 1% to 4% of patients, respectively:
  - Rash
  - Cellulitis
  - Petechiae
  - Urticaria
  - Basal cell carcinoma

- Other events (relationship to drug not established) that were less frequent than 1% include:
  - Acne
  - Hair loss
  - Visual disturbance
  - Depression

- No carcinogenic potential was demonstrated in mice treated subcutaneously for 85 to 99 weeks at doses up to 2000 mcg/kg/day. No carcinogenic potential was demonstrated in rats treated orally for 66 months at doses up to 850 mcg/kg/day. Octreotide acetate did not impair fertility in rats at doses up to 1000 mcg/kg/day, which represents 7x the human exposure based on body surface area.

- 199mm × 590mm

- 57457-245-01

- Drug Administration:
  - The initial dosage is usually 50 mcg administered twice or three times daily. Upward dose titration is frequently required. Dosage may be initiated at 50 mcg t.i.d. Beginning with this low dose may permit adaptation to adverse gastrointestinal effects for patients who will require higher doses. IGF-I (somatomedin C) levels every 2 weeks can be used to guide titration. Alternatively, a single measurement of IGF-I (somatomedin C) level on the specific tumor. Based on diagnosis, measurement of the following substances may be useful in monitoring the progress of disease activity:

- Drug Abuse and Dependence: There is no indication that octreotide acetate has potential for drug dependence or abuse.

- Hematologic:
  - Thrombocytopenia
  - Megakaryocytic hypoplasia
  - Hemolytic anemia
  - Sideropenic anemia
  - Aplastic anemia
  - Hemoglobinuria
  - Hematuria

- Nausea
- Vomiting
- Diarrhea
- Abdominal pain
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- Bowel obstruction
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- Cardiovascular:
  - Hypotension
  - Palpitations
  - Chest pain

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- Pregnancy: Teratogenic Effects. Category B: There are no adequate and well-controlled studies in pregnant women. Reproduction studies have been performed in rats and rabbits at doses up to 10 times the highest recommended human dose and have revealed no evidence of impaired fertility or harm to the fetus due to octreotide acetate. However, small amounts of octreotide may reach the fetus through the placenta. In rats, octreotide acetate produced a decrease in fetal body weight and body length at a maternal dose of 20 mg/kg/day (40 times the human dose on a body surface area basis). The significance of this finding is unknown. There are no adequate and well-controlled studies in pregnant women. It is not known whether octreotide acetate can cause fetal harm when administered to a pregnant woman. Octreotide acetate should be given to pregnant women only if clearly needed.

- In acromegalics, sinus bradycardia (< 50 bpm) developed in 25%; conduction abnormalities occurred in 10% and arrhythmias in 4%.

- Gallbladder abnormalities, especially stones and/or biliary sludge, frequently develop in patients on chronic octreotide acetate therapy (see WARNINGS).

- Vasoactive Intestinal Peptide (VIP) secreting adenomas (watery diarrhea).

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