VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

OCTREOTIDE ACETATE

Effective Date: 1/28/14
Date Developed: 1/28/14 by Catherine Sanders, MD
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Octreotide Acetate mimics natural somatostatin by inhibiting serotonin release, and the secretion of gastrin, VIP, insulin, glucagon, secretin, motilin, and pancreatic polypeptide. Decreases growth hormone and IGF-1 in acromegaly. Octreotide provides more potent inhibition of growth hormone, glucagon, and insulin as compared to endogenous somatostatin. Also suppresses LH response to GnRH, secretion of thyroid-stimulating hormone and decreases splanchnic blood flow.

Pre-Authorization Criteria:
Octreotide is covered for the use of:

1) Controlling symptoms of diarrhea and flushing in patients with metastatic carcinoid tumors
2) Treatment of watery diarrhea associated with vasoactive intestinal peptide-secreting tumors (VIPomas)
3) Treatment of acromegaly

Octreotide is not covered for the of treatment of AIDS-associated diarrhea (including *Cryptosporidiosis*), chemotherapy-induced diarrhea, graft-versus-host disease (GVHD) associated diarrhea, postgastrectomy dumping syndrome; control of bleeding of esophageal varices; second-line treatment for thymic malignancies; Cushing's syndrome (ectopic); insulinomas; small bowel fistulas; islet cell tumors; Zollinger-Ellison syndrome; congenital hyperinsulinism; hypothalamic obesity; treatment of hypoglycemia secondary to sulfonylurea poisoning; treatment of malignant bowel obstruction as these are all unlabeled uses. (See VCHCP policy on coverage of prescription medication for off-label use.)

Dosing: Adult:
Acromegaly:
SubQ, I.V.: Initial: 50 mcg 3 times/day; titrate to achieve growth hormone levels <5 ng/mL or IGF-I (somatomedin C) levels <1.9 units/mL in males and <2.2 units/mL in females. Usual effective dose 100-200 mcg 3 times/day; range 300-1500 mcg/day. Note: Should be withdrawn yearly for a 4-week interval (8 weeks for depot injection) in patients who have received irradiation. Resume if levels increase and signs/symptoms recur.
I.M. depot injection: Patients must be stabilized on subcutaneous octreotide for at least 2 weeks before switching to the long-acting depot. Upon switch: 20 mg I.M. intragluteally every 4 weeks for 3 months, then the dose may be modified based upon response.

Dosage adjustment for acromegaly: After 3 months of depot injections, the dosage may be continued or modified as follows:
GH ≤1 ng/mL, IGF-1 normal, and symptoms controlled: Reduce octreotide depot to 10 mg I.M. every 4 weeks
GH ≤2.5 ng/mL, IGF-1 normal, and symptoms controlled: Maintain octreotide depot at 20 mg I.M. every 4 weeks
GH >2.5 ng/mL, IGF-1 elevated, and/or symptoms uncontrolled: Increase octreotide depot to 30 mg I.M. every 4 weeks
Note: Patients not adequately controlled at a dose of 30 mg may increase dose to 40 mg every 4 weeks. Dosages >40 mg are not recommended.

Carcinoid tumors:
Manufacturer labeling:
SubQ, I.V.: Initial 2 weeks: 100-600 mcg/day in 2-4 divided doses; usual range: 50-750 mcg/day (some patients may require up to 1500 mcg/day)
I.M. depot injection: Patients must be stabilized on subcutaneous octreotide for at least 2 weeks before switching to the long-acting depot. Upon switch: 20 mg I.M. intragluteally every 4 weeks for 2 months, then the dose may be modified based upon response.
NCCN guidelines (Neuroendocrine Tumor v.1.2011):
SubQ: 150-250 mcg 3 times/day; dose and frequency may be increased if needed for symptom control
I.M. depot injection: 20-30 mg every 4 weeks; dose and frequency may be increased if needed for symptom control; SubQ octreotide may be used for breakthrough symptoms
Note: Patients should continue to receive their SubQ injections for the first 2 weeks at the same dose in order to maintain therapeutic levels (some patients may require 3-4 weeks of continued SubQ injections). Patients who experience periodic exacerbations of symptoms may require temporary SubQ injections in addition to depot injections (at their previous SubQ dosing regimen) until symptoms have resolved.
Dosage adjustment for carcinoid tumors: After 2 months of depot injections, the dosage may be continued or modified as follows:
Increase to 30 mg I.M. every 4 weeks if symptoms are inadequately controlled
Decrease to 10 mg I.M. every 4 weeks, for a trial period, if initially responsive to 20 mg dose
Dosage >30 mg is not recommended

VIPomas:
Manufacturer labeling:
SubQ, I.V.: Initial 2 weeks: 200-300 mcg/day in 2-4 divided doses; titrate dose based on response/tolerance. Range: 150-750 mcg/day (doses >450 mcg/day are rarely required)
I.M. depot injection: Patients must be stabilized on subcutaneous octreotide for at least 2 weeks before switching to the long-acting depot. Upon switch: 20 mg I.M. intragluteally every 4 weeks for 2 months, then the dose may be modified based upon response.
NCCN guidelines (Neuroendocrine Tumor, v.1.2011):
SubQ: 150-250 mcg 3 times/day; dose and frequency may be increased if needed for symptom control
I.M. depot injection: 20-30 mg every 4 weeks dose and frequency may be increased if needed for symptom control; SubQ octreotide may be used for breakthrough symptoms

Note: Patients receiving depot injection should continue to receive their SubQ injections for the first 2 weeks at the same dose in order to maintain therapeutic levels (some patients may require 3-4 weeks of continued SubQ injections). Patients who experience periodic exacerbations of symptoms may require temporary SubQ injections in addition to depot injections (at their previous SubQ dosing regimen) until symptoms have resolved.
Dosage adjustment for VIPomas: After 2 months of depot injections, the dosage may be continued or modified as follows:
Increase to 30 mg I.M. every 4 weeks if symptoms are inadequately controlled
Decrease to 10 mg I.M. every 4 weeks, for a trial period, if initially responsive to 20 mg dose
Dosage >30 mg is not recommended

Diarrhea (unlabeled use): I.V.: Initial: 50-100 mcg every 8 hours; increase by 100 mcg/dose at 48-hour intervals; maximum dose: 500 mcg every 8 hours
Diarrhea associated with chemotherapy (unlabeled use):
Low grade or uncomplicated: SubQ: 100-150 mcg every 8 hours (Benson, 2004; Kornblau, 2000)
Severe: Initial: SubQ: 100-150 mcg every 8 hours; may increase to 500-1500 mcg I.V. or SubQ every 8 hours (Kornblau, 2000)
Complicated: I.V., SubQ: Initial: 100-150 mcg 3 times/day or I.V. Infusion: 25-50 mcg/hour; may escalate to 500 mcg 3 times/day until controlled (Benson, 2004)
Diarrhea associated with GVHD (unlabeled use): I.V.: 500 mcg every 8 hours; discontinue within 24 hours of resolution; Maximum duration of therapy if diarrhea is not resolved: 7 days (Kornblau, 2000)
Esophageal varices bleeding (unlabeled use): I.V. bolus: 25-100 mcg (usual bolus dose: 50 mcg) followed by continuous I.V. infusion of 25-50 mcg/hour for 2-5 days; may repeat bolus in first hour if hemorrhage not controlled (Corley, 2001; Erstad, 2001; Garcia-Tsao, 2010)
Hypoglycemia in sulfonylurea poisoning (unlabeled use): SubQ is the preferred route of administration; repeat dosing, dose escalation, or initiation of a continuous infusion may be required in patients who experience recurrent hypoglycemia. Duration of treatment may exceed 24 hours. Optimal care decisions should be made based upon patient-specific details:
SubQ: 50-100 mcg; repeat in 6-12 hours as needed based upon blood glucose concentrations (Braatvedt, 1997; Carr, 2002; Graudins, 1997; Hung, 1997)
I.V.: Doses up to 100-125 mcg/hour have been used successfully (McLaughlin, 2000)
Islet cell tumors (unlabeled use): SubQ: 150-250 mcg 3 times/day or I.M. (depot): 20-30 mg every 4 weeks dose and frequency may be increased if needed for symptom control; SubQ octreotide may be used for breakthrough symptoms (NCCN Neuroendocrine Tumor guidelines v.1.2011)
Malignant bowel obstruction (unlabeled use):
SubQ: 100-300 mcg 2-3 times/day (Mercadante, 2007; NCCN Palliative Care guidelines v.2.2011)
Continuous SubQ/I.V. infusion: 10-40 mcg/hour (NCCN Palliative Care guidelines v.2.2011)

Dosing: Pediatric:
Infants and Children:
Secretory diarrhea (unlabeled use): I.V., SubQ: Doses of 1-10 mcg/kg every 12 hours have been used in children beginning at the low end of the range and increasing by 0.3 mcg/kg/dose at 3-day intervals. Suppression of growth hormone (animal data) is of concern when used as long-term therapy.
Congenital hyperinsulinism (unlabeled use): SubQ: Initial: 2-10 mcg/kg/day; up to 40 mcg/kg/day have been used (Stanley, 1997).
Hypoglycemia in sulfonylurea poisoning (unlabeled use): SubQ is the preferred route of administration; repeat dosing, dose escalation, or initiation of a continuous infusion may be required in patients who experience recurrent

hypoglycemia. Duration of treatment may exceed 24 hours. Optimal care decisions should be made based upon patient-specific details: SubQ: 1-1.5 mcg/kg; repeat in 6-12 hours as needed based upon blood glucose concentrations (Calello, 2005; Glatstein, 2009).

Dosing: Geriatric:
Refer to adult dosing. Elimination half-life is increased by 46% and clearance is decreased by 26%; dose adjustment may be required. Dosing should generally begin at the lower end of dosing range.

Dosing: Renal Impairment:
Nondialysis-dependent renal impairment: No dosage adjustment required
Dialysis-dependent renal impairment: Depot injection: Initial dose: 10 mg I.M. every 4 weeks; titrate based upon response (clearance is reduced by ~50%)
Dosing: Hepatic Impairment:
Patients with established cirrhosis of the liver: Depot injection: Initial dose: 10 mg I.M. every 4 weeks; titrate based upon response.

Dosage Forms: U.S.:
Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
Kit, Intramuscular:
SandoSTATIN LAR Depot: 10 mg, 20 mg, 30 mg
Solution, Injection:
SandoSTATIN: 50 mcg/mL (1 mL); 100 mcg/mL (1 mL)
SandoSTATIN: 200 mcg/mL (5 mL) [contains phenol]
SandoSTATIN: 500 mcg/mL (1 mL)
SandoSTATIN: 1000 mcg/mL (5 mL) [contains phenol]
Generic: 50 mcg/mL (1 mL); 100 mcg/mL (1 mL); 200 mcg/mL (5 mL); 1000 mcg/5 mL (5 mL); 500 mcg/mL (1 mL); 1000 mcg/mL (5 mL)
Solution, Injection [preservative free]:
Generic: 100 mcg/mL (1 mL); 500 mcg/mL (1 mL)

Generic Equivalent Available: U.S.-May be product dependent

Administration:
Regular injection formulation (do not use if solution contains particles or is discolored): Administer SubQ or I.V.; I.V. administration may be I.V. push (undiluted over 3 minutes), intermittent I.V. infusion (over 15-30 minutes), or continuous I.V. infusion (unlabeled route).
SubQ: Use the concentration with smallest volume to deliver dose to reduce injection site pain. Rotate injection site; may bring to room temperature prior to injection.
Depot formulation: Administer I.M. intragluteal (avoid deltoid administration); alternate gluteal injection sites to avoid irritation. Do not administer Sandostatin LAR® intravenously or subcutaneously; must be administered immediately after mixing.
Usual Infusion Concentrations: Adult
I.V. infusion: 500 mcg in 250 mL (concentration: 2 mcg/mL) of D_5W or NS

Compatibility:
Solution: Stable in D_5W, NS; incompatible with fat emulsion 10%; variable stability in TPN (The manufacturer states that octreotide solution is not compatible in TPN solutions due to the formation of a glycosyl octreotide conjugate which may have decreased activity; other sources assign limited compatibility.)
Y-site administration: Compatible: Levofloxacin. Incompatible: Micafungin. Variable (consult detailed reference): Pantoprazole, TPN.
Compatibility in syringe: Incompatible: Dimenhydrinate, pantoprazole.

Adverse Reactions:
>10%: sinus bradycardia, chest pain, fatigue, headache, malaise, fever, dizziness, pruritus, hyperglycemia, abdominal pain, loose stools, nausea, diarrhea, flatulence, cholelithiasis, biliary sludge, constipation, vomiting, biliary duct dilatation, injection site pain, back pain, arthropathy, myalgia, upper respiratory infection, dyspnea, antibodies to octreotide, flu symptoms.
Other Serious Less Common Reactions: ascending cholangitis, biliary obstruction, pancreatitis, arrhythmias, conduction disturbance, syncope, severe edema, CHF exacerbation, hypertension, anaphylaxis, goiter, hypothyroidism, vitamin B12 deficiency, zinc excess, thrombocytopenia.

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