Octreotide: Drug information

(For additional information see "Octreotide: Patient drug information" and see "Octreotide: Pediatric drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

Brand Names: US

SandoSTATIN; SandoSTATIN LAR Depot

Brand Names: Canada

Ocphyl; Octreotide Acetate Omega; Octreotide Injection; Sandostatin; Sandostatin LAR

Pharmacologic Category

Antidiarrheal; Antidote; Somatostatin Analog

Dosing: Adult

Acromegaly:

SubQ, IV: 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 mcg 3 times/day; range: 300 to 1,500 mcg/day. Doses above 300 mcg/day rarely result in additional benefit; if increased dose fails to provide additional benefit, the dose should be reduced. **Note:** Should be withdrawn yearly for a 4-week interval (8 weeks for depot injection) in patients who have received irradiation.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.

IM 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 IM 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 IM every 4 weeks

GH ≤2.5 ng/mL, IGF-1 normal, and symptoms controlled: Maintain octreotide depot at 20 mg IM every 4 weeks

GH >2.5 ng/mL, IGF-1 elevated, and/or symptoms uncontrolled: Increase octreotide depot to 30 mg IM 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:

SubQ, IV: Initial 2 weeks: 100 to 600 mcg/day in 2 to 4 divided doses; usual range: 50 to 750 mcg/day (some patients may require up to 1,500 mcg/day); experience with doses above 750 mcg/day is limited.

IM 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 IM intragluteally every 4 weeks for 2 months, then the dose may be modified based upon response.

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 to 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 IM every 4 weeks if symptoms are inadequately controlled

Decrease to 10 mg IM every 4 weeks, for a trial period, if initially responsive to 20 mg dose

Dosage >30 mg is not recommended

Vasoactive intestinal peptide tumors (VIPomas):

SubQ, IV: Initial 2 weeks: 200 to 300 mcg/day in 2 to 4 divided doses; titrate dose based on response/tolerance. Range: 150 to 750 mcg/day (doses >450 mcg/day are rarely required)

IM 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 IM intragluteally every 4 weeks for 2 months, then the dose may be modified based upon response.

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 to 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 IM every 4 weeks if symptoms are inadequately controlled

Decrease to 10 mg IM every 4 weeks, for a trial period, if initially responsive to 20 mg dose

Dosage >30 mg is not recommended

Carcinoid crisis, prevention (off-label use): Immediate release octreotide solution (Oberg 2004):

Patients controlled with octreotide IM (depot) 20 to 30 mg: SubQ: 250 to 500 mcg within 1 to 2 hours prior to procedure.

Emergency surgery in somatostatin analog-naïve patients with functional neuroendocrine tumors:

IV bolus: 500 to 1000 mcg 1 to 2 hours prior to procedure **or**

SubQ: 500 mcg 1 to 2 hours prior to procedure

Intraoperative use for carcinoid crisis with hypotension: IV: 500 to 1,000 mcg bolus, repeat at 5 minute intervals until symptoms are controlled or IV: 500 to 1,000 mcg bolus followed by 50 to 200 mcg/hour continuous infusion during the procedure.

Postoperative dose (if supplemental doses required during procedure): IV: 50 to 200 mcg/hour continuous infusion for 24 hours, followed by resumption of the preoperative treatment schedule.

Diarrhea (off-label use): IV: Initial: 50 to 100 mcg every 8 hours; increase by 100 mcg/dose at 48-hour intervals; maximum dose: 500 mcg every 8 hours

Diarrhea (refractory) associated with chemotherapy (off-label use):

Low grade or uncomplicated: SubQ: 100 to 150 mcg every 8 hours (Benson 2004; Kornblau 2000)

Severe: Initial: SubQ: 100 to 150 mcg every 8 hours; may increase to 500 to 1500 mcg IV or SubQ every 8 hours (Kornblau 2000)

Complicated: IV, SubQ: Initial: 100 to 150 mcg 3 times/day or IV Infusion: 25 to 50 mcg/hour; may escalate to 500 mcg 3 times/day until controlled (Benson 2004)

Diarrhea associated with acute graft-versus-host disease (GVHD) (off-label use): IV: 500 mcg every 8 hours; discontinue within 24 hours of diarrhea resolution to avoid ileus; Maximum duration of therapy if diarrhea is not resolved: 7 days (Kornblau 2000)

Esophageal varices bleeding (off-label use): IV bolus: 25 to 100 mcg (usual bolus dose: 50 mcg) followed by continuous IV infusion of 25 to 50 mcg/hour for 2 to 5 days; may repeat bolus in first hour if hemorrhage not controlled (Corley 2001; Erstad 2001; Garcia-Tsao 2010)

Gastroenteropancreatic neuroendocrine tumors (off-label use):

IM (depot): 30 mg every 4 weeks until tumor progression or death (Rinke 2009) **or**

SubQ: Initial: 100 to 500 mcg 2 to 4 times daily (usually 150 mcg 3 times daily), may increase to response (symptom control) by doubling the dose every 3 to 4 days or a continuous subQ infusion of 1,000 to 2,000 mcg/day (Oberg 2004) **or**

IM (depot): Assure tolerability by initiating with the SubQ formulation for 3 to 7 days (and continue with SubQ for the first ~14 days after the initial IM depot dose). Then initiate IM (depot): 20 to 30 mg every 28 days (SubQ doses of 200 to 600 mcg/day should receive 20 mg IM and SubQ doses of 750 to 1,500 mcg/day should receive 30 mg IM); IM (depot) range: 20 to 60 mg every 28 days (Oberg 2004).

Hepatorenal syndrome (off-label use): SubQ: Initial: 100 mcg 3 times daily; may increase to 200 mcg 3 times daily (with a goal to increase mean arterial pressure [MAP] by at least 15 mm Hg from baseline) (Angeli 1999; Esrailian 2007; Garcia-Tsao 2009; AASLD [Runyon 2012])

Malignant bowel obstruction (off-label use): SubQ: 200 to 900 mcg/day in 2 to 3 divided doses (Mercadante 2007; Mercadante 2012) or 300 mcg/day by continuous SubQ infusion (Mercadante 2000)

Sulfonylurea-induced hypoglycemia (off-label use): Note: Although octreotide use has been advocated as a first line therapy, indications and dosing for octreotide are not firmly established (Glatstein 2012). Octreotide may reduce the incidence of recurrent hypoglycemia seen with dextrose-

alone therapy (Fasano 2008). In addition, although subcutaneous administration is the preferred route, administration via intravenous bolus and intravenous infusion have also been described in the literature (Barkin 2013; Braatvedt 1997; Carr 2002; Crawford 2004; Dougherty 2010; Dougherty 2013; Fasano 2008; Graudins 1997; Green 2003; Hung 1997; McLaughlin 2000; Mordel 1998). Optimal care decisions should be made based upon patient-specific details. 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.

SubQ: 50 to 75 mcg; repeat every 6 hours as needed based upon blood glucose concentrations (Fasano 2008; Howland 2011)

IV: Doses up to 125 mcg/hour have been used successfully (McLaughlin 2000)

Thymoma/thymic malignancies, advanced (off-label use): SubQ: 500 mcg 3 times daily; evaluate after 2 months, patients with remission (complete or partial) continued octreotide for up to a maximum of 12 months; patients with stable disease continued octreotide and also received prednisone for up to 12 months or until disease progression or unacceptable toxicity (Loehrer 2004).

Dosing: Pediatric

(For additional information see "Octreotide: Pediatric drug information")

Infants and Children:

Congenital hyperinsulinism (off-label use): SubQ: Initial: 2 to 10 mcg/kg/day; up to 40 mcg/kg/day have been used (Stanley 1997).

Secretory diarrhea (off-label use): IV, SubQ: Doses of 1 to 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.

Sulfonylurea-induced hypoglycemia (off-label use): Note: Although octreotide use has been advocated as a first line therapy, indications and dosing for octreotide are not firmly established (Glatstein 2012). Octreotide may reduce the incidence of recurrent hypoglycemia seen with dextrose-alone therapy (Fasano 2008). In addition, although subcutaneous administration is the preferred route, administration via intravenous bolus and intravenous infusion have also been described in the literature (Barkin 2013; Braatvedt 1997; Carr 2002; Crawford 2004; Dougherty 2010; Dougherty 2013; Fasano 2008; Graudins 1997; Green 2003; Hung 1997; McLaughlin 2000; Mordel 1998). Optimal care decisions should be made based upon patient-specific details. 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. SubQ: 1 to 1.25 mcg/kg; repeat in 6 hours as needed based upon blood glucose concentrations (Howland 2011). Children generally need only a single dose (Dougherty 2013).

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

Regular injection (solution):

Mild to severe impairment: There are no dosage adjustments provided in the manufacturer's labeling.

Severe impairment requiring dialysis: There are no specific dosage adjustments provided in the manufacturer's labeling; however, a dosage adjustment may be needed since clearance is reduced by ~50%.

Depot injection:

Mild to severe impairment: No initial dosage adjustment necessary.

Severe impairment requiring dialysis: Initial dose: 10 mg IM every 4 weeks; titrate based upon response (clearance is reduced by ~50%)

Dosing: Hepatic Impairment

Regular injection (solution): There are no dosage adjustments provided in the manufacturer's labeling. Half-life is prolonged and total body clearance is decreased in patients with cirrhosis and fatty liver disease.

Depot injection: Patients with established cirrhosis of the liver: Initial dose: 10 mg IM every 4 weeks; titrate based upon response.

Dosage Forms

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 (US)

May be product dependent

Administration

Regular injection formulation: Administer SubQ or IV; IV administration may be IV push (undiluted over 3 minutes), intermittent IV infusion (over 15 to 30 minutes), or continuous IV infusion (off-label route). In

emergency situations (eg, carcinoid crisis), octreotide may be given as a rapid IV bolus.

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 IM intragluteal (avoid deltoid administration); alternate gluteal injection sites to avoid irritation. For IM administration only; **do not** administer depot formulation (Sandostatin LAR) intravenously or subcutaneously; must be administered immediately after mixing.

Usual Infusion Concentrations: Adult

IV infusion: 500 mcg in 250 mL (concentration: 2 **mcg**/mL) of D5W or NS

Use

Acromegaly:

Injection solution: To reduce blood levels of growth hormone (GH) and insulin-like growth factor 1 (IGF-1) in patients with inadequate response to or who cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses; goal of therapy is to achieve normalization of GH and IGF-1 levels.

LAR depot suspension: Long-term maintenance treatment of acromegaly in patients with an inadequate response to surgery and/or radiotherapy (or for whom surgery/radiotherapy are not options) with a goal of therapy to reduce GH and IGF-1 levels to normal.

Carcinoid tumors:

Injection solution: Management of symptoms (diarrhea and flushing) in patients with metastatic carcinoid tumors.

LAR depot suspension: Long-term treatment of severe diarrhea and flushing episodes associated with metastatic carcinoid tumors.

Vasoactive intestinal peptide-secreting tumors:

Injection solution: Treatment of profuse watery diarrhea associated with vasoactive intestinal peptide-secreting tumors (VIPomas).

LAR depot suspension: Long-term treatment of profuse watery diarrhea associated with VIPomas.

Limitations of use: The effects of octreotide (injection solution and LAR depot suspension) on tumor size, rate of growth, and development of metastases in patients with carcinoid syndrome and VIPomas have not been determined.

Use: Off-Label

Carcinoid crisis (prevention); Diarrhea (refractory or persistent) associated with chemotherapy; Diarrhea associated with graft-versus-host disease (GVHD); Gastroenteropancreatic neuroendocrine tumors (metastatic); Gastroesophageal variceal hemorrhage; Hepatorenal syndrome; Malignant bowel obstruction; Sulfonylurea-induced hypoglycemia; Thymoma/thymic malignancies (advanced); AIDS-associated diarrhea (including Cryptosporidiosis); Congenital hyperinsulinism; Cushing's syndrome (ectopic); Hypothalamic obesity; Postgastrectomy dumping syndrome; Small bowel fistulas; Zollinger-Ellison syndrome

Medication Safety Issues

Sound-alike/look-alike issues:

Octreotide may be confused with lanreotide, pasireotide

SandoSTATIN may be confused with SandIMMUNE, SandoSTATIN LAR, sargramostim, simvastatin

Adverse Reactions

Adverse reactions vary by route of administration and dosage form. Frequency of cardiac, endocrine, and gastrointestinal adverse reactions was generally higher in patients with acromegaly.

>10%:

Cardiovascular: Sinus bradycardia (19% to 25%), chest pain (≤20%; non-depot formulations), palpitations (5% to 15%), peripheral edema (5% to 15%), hypertension (≤13%)

Central nervous system: Fatigue (1% to 32%), headache (6% to 30%), malaise (16% to 20%), dizziness (5% to 20%), anxiety (5% to 15%), confusion (5% to 15%), hypoesthesia (5% to 15%), insomnia (5% to 15%), paresthesia (5% to 15%), rigors (5% to 15%), pain (4% to 15%)

Dermatologic: Pruritus (≤18%), skin rash (15%; depot formulation), diaphoresis (5% to 15%), alopecia (≤13%)

Endocrine & metabolic: Hyperglycemia (2% to 27%), hypothyroidism (≤12%; non-depot formulations)

Gastrointestinal: Diarrhea (34% to 61%), abdominal pain (5% to 61%), loose stools (5% to 61%), nausea (5% to 61%), flatulence (≤38%), cholelithiasis (13% to 38%; length of therapy-dependent), gallbladder sludge (24%; length of therapy-dependent), constipation (9% to 21%), vomiting (4% to 21%), biliary obstruction (duct dilatation: 12%), anorexia (5% to 15%), abdominal cramps (5% to 15%)

Hematologic & oncologic: Anemia (≤15%; non-depot formulations: <1%)

Hypersensitivity: Hypersensitivity reaction (5% to 15%)

Immunologic: Antibody development (≤25%; to octreotide; no efficacy change)

Local: Pain at injection site (2% to 50%; formulation-related)

Neuromuscular & skeletal: Back pain (1% to 27%), arthropathy (8% to 19%), myalgia (≤18%), arthralgia (1% to 15%), weakness (5% to 15%)

Otic: Otalgia (5% to 15%)

Renal: Nephrolithiasis (5% to 15%)

Respiratory: Upper respiratory tract infection (10% to 23%), dyspnea (≤20%; non-depot formulations), flu-like symptoms (1% to 20%), cough (5% to 15%), pharyngitis (5% to 15%), rhinitis (5% to 15%), sinusitis (5% to 15%)

Miscellaneous: Fever (16% to 20%)

1% to 10%:

Cardiovascular: Cardiac conduction disturbance (9% to 10%), cardiac arrhythmia (3% to 9%), angina pectoris (1% to 4%), cardiac failure (1% to 4%), edema (1% to 4%), flushing (1% to 4%), phlebitis (1% to 4%)

Central nervous system: Abnormal gait (1% to 4%), amnesia (1% to 4%), depression (1% to 4%), drowsiness (1% to 4%), hallucination (1% to 4%), hypertonia (1% to 4%), nervousness (1% to 4%), neuralgia (1% to 4%), neuropathy (1% to 4%), vertigo (1% to 4%), voice disorder (1% to 4%)

Dermatologic: Acne vulgaris (1% to 4%), cellulitis (1% to 4%)

Endocrine & metabolic: Goiter (≤8%; non-depot formulations), hypoglycemia (2% to 4%), albuminuria (1% to 4%), hypokalemia (1% to 4%), gout (1% to 4%), cachexia (1% to 4%)

Gastrointestinal: Dyspepsia (4% to 6%), fecal discoloration (4% to 6%), steatorrhea (4% to 6%), tenesmus (4% to 6%), colitis (1% to 4%), diverticulitis (1% to 4%), dysgeusia (1% to 4%), dysphagia (1% to 4%), gastritis (1% to 4%), gastroenteritis (1% to 4%), gingivitis (1% to 4%), glossitis (1% to 4%), malabsorption (fat: 1% to 4%), melena (1% to 4%), stomatitis (1% to 4%), xerostomia (1% to 4%)

Genitourinary: Impotence (1% to 4%), mastalgia (1% to 4%), pollakiuria (1% to 4%; non-depot formulations), urinary incontinence (1% to 4%), urinary tract infection (1% to 4%)

Hematologic & oncologic: Bruise (1% to 4%), hematoma (1% to 4%), hypoproteinemia (1% to 4%)

Infection: Abscess (renal: 1% to 4%), bacterial infection (1% to 4%), candidiasis (1% to 4%), cold symptoms (1% to 4%)

Local: Hematoma at injection site (1% to 4%)

Neuromuscular & skeletal: Hyperkinesia (1% to 4%), tremor (1% to 4%)

Ophthalmic: Blurred vision (1% to 4%), visual disturbance (1% to 4%)

Otic: Tinnitus (1% to 4%)

Respiratory: Bronchitis (1% to 4%), epistaxis (1% to 4%)

<1%, postmarketing, and/or case reports: Adrenocortical insufficiency, amenorrhea, anaphylactic shock, anaphylactoid reaction, aneurysm, aphasia, appendicitis, arthritis, ascites, atrial fibrillation, basal cell carcinoma, Bell's palsy, biliary obstruction, breast carcinoma, cardiac failure, cerebrovascular disease, cholangitis (ascending), cholecystitis, cholestatic hepatitis, cyanocobalamin deficiency, deafness, decreased libido, diabetes insipidus, diabetes mellitus, erythema (with wheal), facial edema, galactorrhea, gastrointestinal hemorrhage, gastrointestinal ulcer, glaucoma, gynecomastia, hematuria, hemiparesis, hemorrhoids, hepatitis, hyperesthesia, hypoxia (children), increased creatine phosphokinase, increased intraocular pressure, increased liver enzymes, increased serum creatinine, intestinal obstruction, intracranial hemorrhage, iron deficiency, ischemia, jaundice, joint effusion, liver steatosis, malignant hyperthermia, menstrual disease (polymenorrhea), migraine, myocardial infarction, necrotizing enterocolitis (neonates), nephrolithiasis, neuritis, nodule (pulmonary), oligomenorrhea, orthostatic hypotension, pancreatitis, pancytopenia, paranoia, paresis, petechia, pituitary apoplexy, pleural effusion, pneumonia, pneumothorax, polyp (gallbladder), prolonged Q-T interval on ECG, pulmonary embolism, pulmonary hypertension, Raynaud’s phenomenon, rectal hemorrhage, renal

failure, renal insufficiency, scotoma, seizure, status asthmaticus, syncope, tachycardia, thrombocytopenia, thrombophlebitis, thrombosis (including retinal vein), urticaria, vaginitis, visual field defect, weight loss

Contraindications

Hypersensitivity to octreotide or any component of the formulation

Warnings/Precautions

Concerns related to adverse effects:

• Abnormal Schillings test: Chronic treatment has been associated with abnormal Schillings test; monitor vitamin B_{12} levels.

• Cholelithiasis: May impair gallbladder function (inhibits gallbladder contractility and decreases bile secretion); monitor patients for cholelithiasis. The incidence of gallbladder stone or biliary sludge increases with a duration of therapy of ≥12 months. Prophylactic cholecystectomy is recommended in patients with gastrointestinal or pancreatic neuroendocrine tumors undergoing abdominal surgery if octreotide treatment is planned (Oberg 2004).

• Glucose regulation: Somatostatin analogs may affect glucose regulation. In type I diabetes, severe hypoglycemia may occur; in type II diabetes or patients without diabetes, hyperglycemia may occur. Insulin and other hypoglycemic medication requirements may change. Octreotide may worsen hypoglycemia in patients with insulinomas; use with caution.

• Local reactions: Mild to moderate injection-site pain (usually lasting 1 hour) may occur with the depot formulation.

• Hypothyroidism: Suppresses secretion of TSH; monitor for hypothyroidism.

• Pancreatitis: May alter absorption of dietary fats; monitor for pancreatitis.

Disease-related concerns:

• Cardiovascular disease: Use with caution in patients with heart failure or concomitant medications that alter heart rate or rhythm; bradycardia, conduction abnormalities, and arrhythmia have been observed in acromegalic and carcinoid syndrome patients. Cardiovascular medication requirements may change.

• Excessive fluid loss: May reduce excessive fluid loss in patients with conditions that cause such a loss; periodic monitoring for elevations in zinc levels is recommended in such patients that are maintained on total parenteral nutrition (TPN).

• Hepatic impairment: Use caution in patients with hepatic impairment; dosage adjustment may be required in patients with established cirrhosis.

• Renal impairment: Use with caution in patients with renal impairment; dosage adjustment may be required in patients receiving dialysis.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

• QTc-prolonging agents: Octreotide may enhance the adverse/toxic effects of other QTc-prolonging agents.

Dosage form specific issues:

• Depot formulation: Do not use depot formulation for the treatment of sulfonylurea-induced hypoglycemia (Dougherty 2010).

• Vehicle used in depot injection (polylactide-co-glycolide microspheres): Has rarely been associated with retinal artery occlusion in patients with abnormal arteriovenous anastomosis (eg, patent foramen ovale).

Special populations:

• Elderly: Dosage adjustment may be necessary; significant increases in elimination half-life have been observed in older adults.

• Females: Therapy may restore fertility; females of childbearing potential should use adequate contraception.

• Pediatric: Postmarketing cases of serious and fatal events, including hypoxia and necrotizing enterocolitis, have been reported with octreotide use in children (usually with serious underlying conditions), particularly in children <2 years of age. In studies with octreotide depot, the incidence of cholelithiasis in children is higher than the reported incidences for adults and efficacy was not demonstrated.

Other warnings/precautions:

• Radiolabeled diagnostic evaluations: Therapy with immediate release octreotide (solution) should be withheld 24 hours prior to administration of radiolabeled somatostatin analogs; the IM (depot) formulation should be withheld at least 2 months before administration of radiolabeled somatostatin analogs (Oberg 2004).

Metabolism/Transport Effects

None known.

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Androgens: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. **Exceptions:** Danazol. *Risk C: Monitor therapy*

Antidiabetic Agents: May enhance the hypoglycemic effect of Hypoglycemia-Associated Agents. *Risk C: Monitor therapy*

Antidiabetic Agents: Hyperglycemia-Associated Agents may diminish the therapeutic effect of Antidiabetic Agents. *Risk C: Monitor therapy*

Bradycardia-Causing Agents: May enhance the bradycardic effect of other Bradycardia-Causing Agents. *Risk C: Monitor therapy*

Bretylium: May enhance the bradycardic effect of Bradycardia-Causing Agents. Bretylium may also enhance atrioventricular (AV) blockade in patients receiving AV blocking agents. *Risk C: Monitor therapy*

Bromocriptine: Somatostatin Analogs may increase the serum concentration of Bromocriptine. Somatostatin Analogs may also delay bromocriptine absorption and time to maximum plasma concentrations. *Risk C: Monitor therapy*

Ceritinib: Bradycardia-Causing Agents may enhance the bradycardic effect of Ceritinib. Management: If this combination cannot be avoided, monitor patients for evidence of symptomatic bradycardia, and closely monitor blood pressure and heart rate during therapy. *Risk X: Avoid combination*

Codeine: Somatostatin Analogs may decrease the metabolism of Codeine. The formation of two major codeine metabolites (morphine and norcodeine) may be impaired by somatostatin analogs. *Risk C: Monitor therapy*

CycloSPORINE (Systemic): Somatostatin Analogs may decrease the serum concentration of CycloSPORINE (Systemic). *Risk D: Consider therapy modification*

Gallium Ga 68 Dotatate: Somatostatin Analogs may diminish the therapeutic effect of Gallium Ga 68 Dotatate. Specifically, a false negative PET scan may occur if Gallium GA 68 Dotatate is used during treatment with somatostatin analogs. Management: Imaging with gallium Ga 68 dotatate positron emission tomography (PET) should be performed just prior to dosing with long-acting somatostatin analogs. Short-acting somatostatin analogs can be used up to 24 hours before imaging with gallium Ga 68 dotatate. *Risk D: Consider therapy modification*

Herbs (Hypoglycemic Properties): May enhance the hypoglycemic effect of Hypoglycemia-Associated Agents. *Risk C: Monitor therapy*

Highest Risk QTc-Prolonging Agents: QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying) may enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. Management: Avoid such combinations when possible. Use should be accompanied by close monitoring for evidence of QT prolongation or other alterations of cardiac rhythm. *Risk D: Consider therapy modification*

Hypoglycemia-Associated Agents: May enhance the hypoglycemic effect of other Hypoglycemia-Associated Agents. *Risk C: Monitor therapy*

Ivabradine: Bradycardia-Causing Agents may enhance the bradycardic effect of Ivabradine. *Risk C: Monitor therapy*

Lacosamide: Bradycardia-Causing Agents may enhance the AV-blocking effect of Lacosamide. *Risk C: Monitor therapy*

MAO Inhibitors: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. *Risk C: Monitor therapy*

MiFEPRIStone: May enhance the QTc-prolonging effect of QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying). Management: Though the drugs listed here have uncertain QT-prolonging effects, they all have some possible association with QT prolongation and should generally be avoided when possible. *Risk D: Consider therapy modification*

Moderate Risk QTc-Prolonging Agents: QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying) may enhance the QTc-prolonging effect of Moderate Risk QTc-Prolonging Agents. *Risk C: Monitor therapy*

Pegvisomant: Somatostatin Analogs may enhance the adverse/toxic effect of Pegvisomant. Specifically, this combination may increase the risk for significant elevations of liver enzymes. *Risk C: Monitor*

therapy

Pegvisomant: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. *Risk C: Monitor therapy*

Prothionamide: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. *Risk C: Monitor therapy*

Quinolone Antibiotics: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. Quinolone Antibiotics may diminish the therapeutic effect of Blood Glucose Lowering Agents. Specifically, if an agent is being used to treat diabetes, loss of blood sugar control may occur with quinolone use. *Risk C: Monitor therapy*

Ruxolitinib: May enhance the bradycardic effect of Bradycardia-Causing Agents. Management: Ruxolitinib Canadian product labeling recommends avoiding use with bradycardia-causing agents to the extent possible. *Risk C: Monitor therapy*

Salicylates: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. *Risk C: Monitor therapy*

Selective Serotonin Reuptake Inhibitors: May enhance the hypoglycemic effect of Blood Glucose Lowering Agents. *Risk C: Monitor therapy*

Telotristat Ethyl: Octreotide may decrease the serum concentration of Telotristat Ethyl. Management: Administer short-acting octreotide at least 30 minutes after administration of telotristat ethyl and monitor for decreased telotristat ethyl efficacy. *Risk D: Consider therapy modification*

Tofacitinib: May enhance the bradycardic effect of Bradycardia-Causing Agents. *Risk C: Monitor therapy*

Food Interactions Octreotide may alter absorption of dietary fats. Management: Administer injections between meals to decrease GI effects.

Pregnancy Risk Factor B (show table)

Pregnancy Implications Adverse events have not been observed in animal reproduction studies. Octreotide crosses the placenta and can be detected in the newborn at delivery (Caron 1995; Fassnacht 2001; Maffei 2010); data concerning use in pregnancy is limited. In case reports of acromegalic women who received normal doses of octreotide during pregnancy, no congenital malformations were reported. Because normalization of IGF-1 and GH may restore fertility in women with acromegaly, women of childbearing potential should use adequate contraception during treatment. Long-acting formulations should be discontinued ~2 months prior to a planned pregnancy; use short acting octreotide as needed until conception. Octreotide therapy may be considered in pregnant women with worsening symptoms if needed. Monitoring of IGF-1 and/or GH is not recommended during pregnancy (Katznelson 2014).

Breast-Feeding Considerations Octreotide is excreted in breast milk. In a case report, a woman was taking octreotide SubQ in doses up to 2400 mcg/day prior to and throughout pregnancy. Octreotide was measurable in the colostrum in concentrations similar to those in the maternal serum (Maffei 2010); however, oral absorption of octreotide is considered to be poor (Battershill, 1989). The manufacturer recommends that caution be exercised when administering octreotide to nursing women.

Dietary Considerations Schedule injections between meals to decrease GI effects. May alter absorption of dietary fats.

Monitoring Parameters

Acromegaly: Growth hormone, somatomedin C (IGF-1)

Carcinoid: 5-HIAA, plasma serotonin and plasma substance P

VIPomas: Vasoactive intestinal peptide

Chronic therapy: Thyroid function (baseline and periodic), vitamin B_{12} level, blood glucose, glycemic control and antidiabetic regimen (patients with diabetes mellitus), cardiac function (heart rate, ECG), zinc level (patients with excessive fluid loss maintained on TPN)

Reference Range Vasoactive intestinal peptide: <75 ng/L; levels vary considerably between laboratories

Mechanism of Action 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.

Pharmacodynamics/Kinetics

Duration: SubQ: 6 to 12 hours; when using Sandostatin LAR Depot formulation, steady-state levels are achieved after 3 injections (3 months of therapy)

Absorption: SubQ: Rapid and complete; IM (depot formulation): Released slowly (via microsphere degradation in the muscle)

Distribution: V_d: 14 L (21.6 ± 8.5 L in acromegaly)

Protein binding: 65%, primarily to lipoprotein (41% in acromegaly)

Metabolism: Extensively hepatic

Bioavailability: SubQ: 100%; IM: 60% to 63% of SubQ dose

Half-life elimination: 1.7 to 1.9 hours; Increased in elderly patients; Cirrhosis: Up to 3.7 hours; Fatty liver disease: Up to 3.4 hours; Renal impairment: Up to 3.1 hours

Time to peak, plasma: SubQ: 0.4 hours (0.7 hours acromegaly); IM: 1 hour

Excretion: Urine (32% as unchanged drug)

Clearance: Adults: 10 L/hour; Adults with acromegaly: 18 L/hour

Pricing: US

Kit (SandoSTATIN LAR Depot Intramuscular)

10 mg (1): $3396.86

20 mg (1): $4450.48

30 mg (1): $6664.27

Solution (Octreotide Acetate Injection)

50 mcg/mL (1 mL): $4.80

100 mcg/mL (1 mL): $7.80

200 mcg/mL (5 mL): $81.60

500 mcg/mL (1 mL): $42.00

1000 mcg/mL (5 mL): $288.00

Solution (SandoSTATIN Injection)

50 mcg/mL (1 mL): $16.61

100 mcg/mL (1 mL): $32.22

200 mcg/mL (5 mL): $332.10

500 mcg/mL (1 mL): $155.39

1000 mcg/mL (5 mL): $1634.11

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names Cryostatin (CR, DO, GT, HN, MX, NI, PA, SV); Nomactril (MX); Octide (ID, TW); Octride (CO, LK, PH); Oktra (UA); Proclose (CR, DO, GT, HN, MX, NI, PA, SV); Sandostatin (AE, AR, AT, AU, BD, BG, BH, BR, CH, CL, CN, CY, CZ, DE, DK, EE, EG, ES, FI, GB, GR, HK, HN, HR, ID, IE, IL, IN, IQ, IR, IS, JO, JP, KR, KW, LB, LK, LT, LU, LV, LY, MT, MY, NO, NZ, OM, PE, PH, PK, PL, PY, QA, RO, RU, SA, SE, SG, SI, SK, SY, TH, TR, TW, UY, VE, VN, YE); Sandostatin LAR (AE, AR, AU, BG, BH, BR, CH, CL, CN, CU, CY, EE, ES, HR, ID, IL, IS, JP, KR, LB, LK, LT, LU, LV, MT, MY, NO, NZ, PE, PH, PY, RO, SA, SE, SG, SI, SK, TH, TW, UY, VN); Sandostatina (IT, MX, PT); Sandostatina LAR (CO); Sandostatine (BE, FR, NL); Sandostatyn (UA); Sandostatyn LAR (UA)

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