DRUG NAME: Lanreotide

SYNONYM(S): lanreotide acetate,[1] SOMATULINE AUTOGEL®,[1] SOMATULINE DEPOT®[2,3]

COMMON TRADE NAME(S): SOMATULINE®

CLASSIFICATION: synthetic somatostatin analogue

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Lanreotide is a synthetic octapeptide analogue of somatostatin, an endogenous peptide present in several areas of the central nervous system and GI tract.[1] It has inhibitory effects on different cell types and on endocrine, neuroendocrine, and exocrine mechanisms.[1] It has high affinity for Type 2 and Type 5 somatostatin receptors (found in the anterior pituitary gland and in the pancreas) and lower affinity for Type 1, 3, and 4 receptors, conferring relative specificity of action on growth hormone (GH) secretion.[1,2] Its predominant pharmacological effect is to reduce GH and age-adjusted insulin-like growth factor 1 (IGF-1) levels in a dose-dependent manner.[1,2] It also inhibits basal secretion of several gastric enzymes and postprandial secretion of pancreatic polypeptide, gastrin, and cholecystokinin.[2] Lanreotide is cell cycle phase-nonspecific.[1,2] Lanreotide is not an immunosuppressive agent.[1]

PHARMACOKINETICS:

Absorption	69-83% bioavailable following deep SC injection[1,3]; steady state plasma concentration[4]: 60 mg dose – 2.4 mcg/L, 90 mg dose – 3.4 mcg/L, 120 mg dose – 4.5 mcg/L	
	time to peak plasma concentration	7-12 h
Distribution	limited extravascular distribution	
	cross blood brain barrier?	no information found
	volume of distribution	0.2 L/kg
	plasma protein binding	78-83%
Metabolism	metabolized extensively in the GI tract following biliary excretion	
	active metabolite(s)	no information found
	inactive metabolite(s)	no information found
Excretion	primarily biliary excretion; patients with severe renal impairment show a 2-fold decrease in total serum clearance, with a consequent increase in half-life and AUC; in patients with hepatic impairment, volume of distribution, mean residence time, AUC, and half-life were all increased; clearance was reduced by 30% only in moderate to severe hepatic impairment	
	urine[1,3]	<1-5%
	feces[1]	<0.5%
	terminal half life[1,3]	23-36 days
	clearance[5]	552 L/day
Elderly	pharmacokinetics differ but no dose adjustment necessary	

Adapted from standard reference[1] unless specified otherwise.

USES:

Primary uses:
*Pituitary tumour
*Neuroendocrine tumour
*Carcinoid syndrome

Other uses:

*Health Canada approved indication

SPECIAL PRECAUTIONS:

Contraindications:
- history of hypersensitivity reaction to lanreotide, somatostatin, or related peptides e.g., octreotide[1]
- complicated, untreated lithiasis of the bile ducts[1]

Caution:
- ***Loss of blood glucose control*** (hypoglycemia or hyperglycemia) can occur.[1,2] Monitor blood glucose when treatment is initiated and when dose is changed.[1,2] Diabetic patients may require treatment adjustments[1,2] and insulin requirements may be reduced in insulin-dependent patients.[1]
- ***Absorption*** of oral medications may be reduced.[1]
- ***Reduced gall bladder motility*** may occur, and may lead to formation of gall stones.[1] Gall bladder ultrasonography is advised at the start of treatment and periodically thereafter.[1,2]
- ***Bradycardia*** may occur in patients with or without existing cardiac disorders[1,2]; monitor heart rate.[1] Initiate with caution in patients with pre-existing bradycardia.[2]

Carcinogenicity: no information found

Mutagenicity: Non-mutagenic in Ames test and mammalian *in vitro* mutation test. Lanreotide is non-clastogenic in mammalian *in vitro* and *in vivo* chromosome tests.[1]

Fertility: no information found

Pregnancy: In animal studies, a transitory growth retardation of offspring was reported. No teratogenic effects have been observed.[6]

Breastfeeding is not recommended due to the potential secretion into breast milk.[1,2]

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 2% of patients in the product monograph or pivotal trials, and/or determined to be clinically important.[7]

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood/bone marrow/ febrile neutropenia	anemia (3-14%)[1,3]
	leukopenia (≤3%)
cardiovascular (arrhythmia)	***bradycardia*** (3-18%)[1,3]; monitoring recommended in patients with existing cardiac disorders[1]
cardiovascular (general)	aortic valve incompetence (≤3%)
	hypertension (1-6%)[1,2]
	heart murmur (≤3%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	heart valve disorders (≤3%)
	myocardial infarction (≤3%)
constitutional symptoms	fatigue (2-6%)
	malaise (≤3%)
	weight decrease (4-11%)[1,3]
dermatology/skin	*extravasation hazard: none*[8]
	alopecia (5-11%)
	hair disorder, not otherwise specified (≤3%)
	injection site induration (5%)[3]
	injection site mass (2-9%)[1,3]
	injection site reaction (≤22%)[1-3]
	nail disorder (≤4%)
gastrointestinal	*emetogenic potential: rare*[9]
	anorexia (≤3%)
	constipation (2-8%)[1-3]
	diarrhea (22-65%)[1,3]
	dyspepsia (1-6%)
	flatulence (4-14%)[1,3]
	loose stools (6%)[3]
	nausea (3-11%)[1,3]
	vomiting (≤7%)[1-3]
hepatobiliary/pancreas	***cholelithiasis and/or biliary sludge*** (12-24%)[1,2]; incidence may be due to dose or duration of therapy[2]
	gall bladder disorder (3-7%)
metabolic/laboratory	hypercholesterolemia (≤4%)
	hyperglycemia (3-7%)
musculoskeletal	***arthralgia*** (1-8%)
neurology	dizziness (≤4%)
	vertigo (≤3%)
pain	***abdominal pain*** (7-19%)[1,3]
	back pain (≤4%)
	chest pain (≤3%)
	headache (≤7%)[1-3]
	injection site pain (5-9%)
pulmonary	dyspnea (≤3%)

Adapted from standard reference[1] unless specified otherwise.

INTERACTIONS:

AGENT	EFFECT	MECHANISM	MANAGEMENT
bromocriptine[1,2]	possible increase in availability of bromocriptine	unknown	monitor for increased effect of bromocriptine and adjust dose accordingly
cyclosporine[1,2]	decreased blood levels of cyclosporin	unknown	monitor cyclosporine levels and adjust dose accordingly
oral medications[1]	intestinal absorption of co-administered medications may be reduced	effect of lanreotide on the gastrointestinal tract	monitor for reduced effect; adjust doses as necessary
vitamin K[1]	no interaction		

Limited data suggest that substrates of the P450 system may be cleared less rapidly, possibly due to the suppression of growth hormone; medications with a low therapeutic index and which are metabolized by CYP 3A4 should be used with caution.[1,2]

SUPPLY AND STORAGE:

***Injection*:** Ipsen Biopharmaceuticals Canada Inc. supplies lanreotide acetate as an extended release preparation in 60 mg/0.5 mL, 90 mg/0.5 mL, and 120 mg/0.5 mL pre-filled syringes. Refrigerate. Store in original packaging.[6]

Additional information: Remove from fridge 30 minutes prior to administration. Keep syringe in laminated pouch until needed.[6]

SOLUTION PREPARATION AND COMPATIBILITY:

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BC Cancer administration guideline noted in ***bold***, ***italics***

Subcutaneous	***deep SC*** into the superior external quadrant of the buttock[1-3] • when self-administration is necessary, injection can be given in upper outer thigh[6]
Intramuscular	no information found
Direct intravenous	no information found
Intermittent infusion	no information found
Continuous infusion	no information found
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response, and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

***Adults*:**

BC Cancer usual dose noted in ***bold, italics***

	Cycle Length:	
Subcutaneous:	***4 weeks***[6,10,11]:	***120 mg*** (range 60-120 mg) ***deep SC for one dose on day 1***
	4 weeks[1-3]:	90 mg deep SC for one dose on day 1 (for 3 months, then adjusted dose based on GH and IGF-1 levels as follows): • GH >2.5 ng/mL, IGF-1 elevated, and/or clinical symptoms uncontrolled: increase to 120 mg every 4 weeks • GH >1 to ≤2.5 ng/mL, IGF-1 normal, and clinical symptoms controlled: maintain dose at 90 mg every 4 weeks • GH ≤1 ng/mL, IGF-1 normal, and clinical symptoms controlled: reduce dose to 60 mg every 4 weeks Thereafter, adjust dose according to response (i.e., reduction in symptoms and/or GH levels and/or IGF-1 levels).
Concurrent radiation:	no information found	
Dosage in myelosuppression:	modify according to protocol by which patient is being treated; if no guidelines available, refer to Appendix "Dosage Modification for Myelosuppression"	
Dosage in renal failure:	no dose adjustment is usually required; starting dose may be reduced to 60 mg[1,2]	
Dosage in hepatic failure:	no dose adjustment is usually required; starting dose may be reduced to 60 mg[1,2]	
Dosage in dialysis:	no information found	

Children:

Subcutaneous:	no information found; use in children cannot be advised.[1]

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