

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 reference¹ unless specified otherwise.**USES:****Primary uses:**

*Pituitary tumour

*Health Canada approved indication

Other uses:

SPECIAL PRECAUTIONS:**Contraindications:**

- history of hypersensitivity reaction to lanreotide, somatostatin, or related peptides e.g., octreotide¹
- complicated, untreated lithiasis of the bile ducts¹

Caution:

- **Loss of blood glucose control** can occur: either hypoglycemia or hyperglycemia.^{1,2} Monitor blood glucose when treatment is initiated and when dose is changed.^{1,2} Diabetics may need their treatments adjusted.^{1,2} 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.¹

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

Fertility: No human data found.

Pregnancy: FDA Pregnancy Category C.³ Studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.

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.⁶

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in bold, italics	
blood/bone marrow/ febrile neutropenia	anemia (3-14%) ^{1,3}
	leukopenia (\leq 3%)
cardiovascular (arrhythmia)	bradycardia (3-18%) ^{1,3} ; monitoring recommended in patients with existing cardiac disorders ¹
cardiovascular (general)	aortic valve incompetence (\leq 3%)
	hypertension (1-6%) ^{1,2}
	heart murmur (\leq 3%)
	heart valve disorders (\leq 3%)
constitutional symptoms	myocardial infarction (\leq 3%)
	fatigue (2-6%)
	malaise (\leq 3%)
	weight decrease (4-11%) ^{1,3}

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

Adapted from standard reference¹ 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	no interaction ¹		

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: Tercica supplies lanreotide acetate as 60 mg/0.3 mL, 90 mg/0.3 mL, and 120 mg/0.5 mL pre-filled syringes containing a supersaturated solution.^{1,2} Refrigerate.¹ Store in original packaging.¹ Syringes may be allowed to reach room temperature (about 30 minutes) prior to administration.² The needle cover contains dry natural rubber (latex).²

SOLUTION PREPARATION AND COMPATIBILITY:

Additional information: the only excipient is water for injection¹

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BCCA administration guideline noted in **bold, italics**

Subcutaneous	<i>deep SC into the superior external (upper outer) quadrant of the buttock¹⁻³. Alternate between left and right buttocks.^{2,3} Insert needle at an angle perpendicular to the skin.² Do not fold skin prior to administration.^{2,3}</i>
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:

BCCA usual dose noted in ***bold, italics***

	Cycle Length:	
<i>Subcutaneous:</i>	4 weeks ¹⁻³ :	<i>90 mg deep SC every 4 weeks for 3 months, then adjusted dose based on GH and IGF-1 levels:</i>
		<ul style="list-style-type: none"> • 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.
<i>Concurrent radiation:</i>		no information found
<i>Dosage in myelosuppression:</i>		modify according to protocol by which patient is being treated; if no guidelines available, refer to Appendix 6 "Dosage Modification for Myelosuppression"
<i>Dosage in renal failure:</i>		no dose adjustment is usually required; starting dose may be reduced to 60 mg ^{1,2}
<i>Dosage in hepatic failure:</i>		no dose adjustment is usually required; starting dose may be reduced to 60 mg ^{1,2}
<i>Dosage in dialysis:</i>		no information found

Children:

Subcutaneous: No information found. Use in children cannot be advised.¹

REFERENCES:

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4. Bronstein M, Musolino N, Jallad R, et al. Pharmacokinetic profile of lanreotide Autogel in patients with acromegaly after four deep subcutaneous injections of 60, 90 or 120 mg every 28 days. *Clin.Endocrinol.(Oxf)* 2005;63(5):514-519.
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