Lanreotide:
Somatuline® Depot; Lanreotide*
(Subcutaneous)

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I. Length of Authorization

Initial coverage will be for three months and is eligible for renewal for six months.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Somatuline Depot/Lanreotide 60 mg/0.2 mL prefilled syringe: 1 syringe every 28 days
- Somatuline Depot/Lanreotide 90 mg/0.3 mL prefilled syringe: 1 syringe every 28 days
- Somatuline Depot/Lanreotide 120 mg/0.5 mL prefilled syringe: 1 syringe every 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

All Indications

- 120 billable (120 mg) units every 28 days

III. Initial Approval Criteria [1,2,3]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria

- Patient has not received a long-acting somatostatin analogue (e.g., Octreotide LAR depot, Lanreotide SR, Lanreotide auto-gel, pasireotide LAR depot, etc.) within the last 4 weeks; **AND**

Acromegaly † Φ [1,2,,5,6]

- Patient's diagnosis is confirmed by elevated (age-adjusted) or equivocal serum IGF-1 as well as inadequate suppression of growth hormone (GH) after a glucose load; **AND**
- Patient has documented inadequate response to surgery and/or radiotherapy or it is not an option for the patient; **AND**
- Patient's tumor has been visualized on imaging studies (i.e., MRI or CT-scan); **AND**
- Baseline GH and IGF-1 blood levels (renewal will require reporting of current levels); **AND**
- Will not be used in combination with oral octreotide

Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs) † Φ [1,2]

- Patient has unresectable, locally advanced or metastatic disease; **AND**
- Patient has non-functioning tumors without hormone-related symptoms; **AND**
- Patient has well or moderately differentiated disease

Carcinoid Syndrome † [1,2,3]

- Patient has documented neuroendocrine tumors with a history of carcinoid syndrome (flushing and/or diarrhea); **AND**
  - Used to reduce the frequency of short-acting somatostatin analog rescue therapy; **OR**
  - Used for treatment and/or control of symptoms

Neuroendocrine and Adrenal Tumors (e.g., GI Tract, Lung, Thymus, Pancreas, and Pheochromocytoma/Paraganglioma) ‡ [1,2,3,8]

- Used as primary treatment for unresected primary gastrinoma; **OR**
- Used for locoregional unresectable bronchopulmonary or thymic disease as primary therapy or as subsequent therapy if progression on first-line therapy (including disease progression on prior treatment with lanreotide in patients with functional tumors); **AND**
  - Used for management of hormone symptoms and/or somatostatin receptor positive disease determined by imaging (i.e., 68Ga-dotatate imaging PET/CT or PET/MRI or somatostatin receptor scintigraphy); **OR**
- Patient has distant metastatic bronchopulmonary or thymic disease; **AND**
  - Used for somatostatin receptor positive disease and/or symptomatic hormonal disease if clinically significant tumor burden and low grade (typical) histology OR evidence of progression OR intermediate grade (atypical histology); **AND**
    - Used as primary therapy or as subsequent therapy if progression on first-line therapy (including disease progression on prior treatment with lanreotide in patients with functional tumors); **OR**
  - Used for somatostatin receptor positive disease and/or hormonal symptoms if asymptomatic with low tumor burden and low grade (typical) histology; **OR**
  - Used for somatostatin receptor positive disease and/or chronic cough/dyspnea that is not responsive to inhalers with multiple lung nodules or tumorlets and evidence of diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH); **OR**
- Used for the management of locoregional advanced or distant metastatic disease of the gastrointestinal tract; **AND**
  - Patient is asymptomatic with a low tumor burden; **OR**
  - Patient with a clinically significant tumor burden; **OR**
  - Patient has disease progression and is not already receiving lanreotide; **OR**

- Patient has disease progression with functional tumors and will be continuing treatment with lanreotide; **OR**

- Used to manage symptoms related to hormone hypersecretion of locoregional neuroendocrine tumors of the pancreas (well differentiated grade 1/2); **AND**
  - Patient has gastrinoma, glucagonoma, or VIPoma; **OR**
- Used for tumor control of locoregional advanced and/or distant metastatic neuroendocrine tumors of the pancreas (well differentiated grade 1/2 – Gastrinoma, Glucagonoma, Insulinoma, VIPoma) [*****NOTE:** for insulinoma ONLY, patient must have somatostatin-receptor positive disease]; **AND**
  - Patient is asymptomatic with a low tumor burden and stable disease; **OR**
  - Patient is symptomatic; **OR**
  - Patient has a clinically significant tumor burden; **OR**
  - Patient has clinically significant progression and is not already receiving lanreotide; **OR**
- Patient has unresectable locally advanced or metastatic neuroendocrine tumors (well differentiated grade 3); **AND**
  - Patient has favorable biology (e.g., relatively low Ki-67 [<55%], somatostatin receptor-positive disease); **OR**
- Patient has pheochromocytoma or paraganglioma; **AND**
  - Patient has symptomatic locally unresectable somatostatin receptor-positive disease; **OR**
  - Patient has distant metastatic disease

**Lanreotide was approved by the FDA as a 505(b) (2) NDA of the innovator product, Somatuline Depot (lanreotide) and thus should NOT be considered therapeutically interchangeable (i.e. not suitable for substitution) for other non-approved indications.*

† FDA Approved Indication(s), ‡ Compendia Approved Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,2,3,8]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: formation of gallstones, cardiovascular abnormalities (bradycardia, sinus bradycardia, and hypertension), uncontrolled blood glucose abnormalities (hyperglycemia or hypoglycemia), thyroid disorders (hypothyroidism), etc.; **AND**

Acromegaly

- Disease response as indicated by an improvement in signs and symptoms compared to baseline; **AND**
  - Reduction of growth hormone (GH) by random testing to < 1.0 mcg/L; **OR**
  - Age-adjusted normalization of serum IGF-1

Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)

- Disease response with treatment as indicated by an improvement in symptoms including reduction in symptomatic episodes (such as diarrhea, rapid gastric dumping, flushing, bleeding, etc.) and/or stabilization of glucose levels and/or decrease in size of tumor or tumor spread

Carcinoid Syndrome

- Disease response with treatment as indicated by reduction in use of short-acting somatostatin analog rescue medication (e.g., octreotide) and a decrease in the frequency of diarrhea and flushing events, when compared to baseline

Neuroendocrine and Adrenal Tumors (e.g., GI Tract, Lung, Thymus, Pancreas, and Pheochromocytoma/Paraganglioma)

- Disease response with treatment as indicated by an improvement in symptoms including reduction in symptomatic episodes (such as diarrhea, rapid gastric dumping, flushing, bleeding, etc.) and/or stabilization of glucose levels and/or decrease in size of tumor or tumor spread; **OR**
- Patient has had disease progression and therapy will be continued in patients with functional tumors

V. Dosage/Administration [1,2,8]

Indication	Dose
Acromegaly	▪ Recommended starting dose is 90 mg by deep subcutaneous injection every 4 weeks for 3 months, adjusted thereafter based on GH and/or IGF-1 levels: – GH >1 to ≤ 2.5 ng/mL, IGF-1 normal and clinical symptoms controlled: maintain Somatuline Depot dose at 90 mg every 4 weeks – GH > 2.5 ng/mL, IGF-1 elevated and/or clinical symptoms uncontrolled, increase Somatuline Depot dose to 120 mg every 4 weeks – GH ≤ 1 ng/mL, IGF-1 normal and clinical symptoms controlled: reduce Somatuline Depot dose to 60 mg every 4 weeks

	▪ *<u>Renal and Hepatic Impairment</u>: Initial dose is 60 mg every 4 weeks for 3 months in moderate and severe renal or hepatic impairment, then adjust thereafter based on GH and/or IGF-1 levels.*
GEP-NETs; Carcinoid Syndrome	▪ 120 mg administered every 4 weeks by deep subcutaneous injection
Neuroendocrine & Adrenal Tumors (GI Tract, Lung, Thymus, Pancreas, & Pheochromocytoma/ Paraganglioma)	▪ Dose range of 90 mg to 120 mg every 4 weeks

VI. Billing Code/Availability Information

<u>HCPCS Code:</u>

- J1930 – Injection, lanreotide, 1 mg; 1 billable unit = 1 mg *(Somatuline Depot only)*
- J3490 – Unclassified drugs *(Lanreotide branded product only)*
- C9399 – Unclassified drugs or biologicals *(Lanreotide branded product only)*

<u>NDC:</u>

- Somatuline Depot 60 mg/0.2 mL prefilled syringe: 15054-1060-xx
- Somatuline Depot 90 mg/0.3 mL prefilled syringe: 15054-1090-xx
- Somatuline Depot 120 mg/0.5 mL prefilled syringe: 15054-1120-xx
- Lanreotide Depot 60 mg/0.2 mL prefilled syringe: 69097-0880-xx
- Lanreotide Depot 90 mg/0.3 mL prefilled syringe: 69097-0890-xx
- Lanreotide Depot 120 mg/0.5 mL prefilled syringe: 69097-0870-xx

VII. References

1. Somatuline Depot [package insert]. Signes, France; Ipsen Pharma Biotech; June 2019. Accessed March 2022.
2. Lanreotide [package insert]. Warren, NJ; Cipla, Inc.; March 2022. Accessed March 2022.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for lanreotide. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2022.

4. Giustina A, Chanson P, Kleinberg D, et al. Expert consensus document: A consensus on the medical treatment of acromegaly. Nat Rev Endocrinol. 2014 Apr; 10(4):243-8. doi: 10.1038/nrendo.2014.21. Epub 2014 Feb 25.
5. Katznelson L, Laws ER Jr, Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014 Nov; 99(11):3933-51. doi: 10.1210/jc.2014-2700. Epub 2014 Oct 30.
6. Fleseriu M, Biller BMK, Freda PU, et al. A Pituitary Society update to acromegaly management guidelines. Pituitary 24, 1–13 (2021). https://doi.org/10.1007/s11102-020-01091-7.
7. Giustina A, Barkhoudarian G, Beckers A et al. Multidisciplinary management of acromegaly: A consensus. Rev Endocr Metab Disord 21, 667–678 (2020). https://doi.org/10.1007/s11154-020-09588-z.
8. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Neuroendocrine and Adrenal Tumors. Version 4.2021. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2022.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C25.4	Malignant neoplasm of endocrine pancreas
C7A.00	Malignant carcinoid tumor of unspecified site
C7A.010	Malignant carcinoid tumor of the duodenum
C7A.011	Malignant carcinoid tumor of the jejunum
C7A.012	Malignant carcinoid tumor of the ileum
C7A.019	Malignant carcinoid tumor of the small intestine, unspecified portion
C7A.020	Malignant carcinoid tumor of the appendix
C7A.021	Malignant carcinoid tumor of the cecum
C7A.022	Malignant carcinoid tumor of the ascending colon
C7A.023	Malignant carcinoid tumor of the transverse colon
C7A.024	Malignant carcinoid tumor of the descending colon
C7A.025	Malignant carcinoid tumor of the sigmoid colon
C7A.026	Malignant carcinoid tumor of the rectum
C7A.029	Malignant carcinoid tumor of the large intestine, unspecified portion

ICD-10	ICD-10 Description
C7A.090	Malignant carcinoid tumor of the bronchus and lung
C7A.091	Malignant carcinoid tumor of the thymus
C7A.092	Malignant carcinoid tumor of the stomach
C7A.093	Malignant carcinoid tumor of the kidney
C7A.094	Malignant carcinoid tumor of the foregut, unspecified
C7A.095	Malignant carcinoid tumor of the midgut, unspecified
C7A.096	Malignant carcinoid tumor of the hindgut, unspecified
C7A.098	Malignant carcinoid tumors of other sites
C7A.1	Malignant poorly differentiated neuroendocrine tumors
C7A.8	Other malignant neuroendocrine tumors
C7B.00	Secondary carcinoid tumors, unspecified site
C7B.01	Secondary carcinoid tumors of distant lymph nodes
C7B.02	Secondary carcinoid tumors of liver
C7B.03	Secondary carcinoid tumors of bone
C7B.04	Secondary carcinoid tumors of peritoneum
C7B.09	Secondary carcinoid tumors of other sites
C7B.8	Other secondary neuroendocrine tumors
C74.10	Malignant neoplasm of medulla of unspecified adrenal gland
C74.11	Malignant neoplasm of medulla of right adrenal gland
C74.12	Malignant neoplasm of medulla of left adrenal gland
C74.90	Malignant neoplasm of unspecified part of unspecified adrenal gland
C74.91	Malignant neoplasm of unspecified part of right adrenal gland
C74.92	Malignant neoplasm of unspecified part of left adrenal gland
C75.5	Malignant neoplasm of aortic body and other paraganglia
D3A.00	Benign carcinoid tumor of unspecified site
D3A.010	Benign carcinoid tumor of the duodenum
D3A.011	Benign carcinoid tumor of the jejunum
D3A.012	Benign carcinoid tumor of the ileum
D3A.019	Benign carcinoid tumor of the small intestine, unspecified portion
D3A.020	Benign carcinoid tumor of the appendix
D3A.021	Benign carcinoid tumor of the cecum
D3A.022	Benign carcinoid tumor of the ascending colon
D3A.023	Benign carcinoid tumor of the transverse colon

ICD-10	ICD-10 Description
D3A.024	Benign carcinoid tumor of the descending colon
D3A.025	Benign carcinoid tumor of the sigmoid colon
D3A.026	Benign carcinoid tumor of the rectum
D3A.029	Benign carcinoid tumor of the large intestine, unspecified portion
D3A.090	Benign carcinoid tumor of the bronchus and lung
D3A.091	Benign carcinoid tumor of the thymus
D3A.092	Benign carcinoid tumor of the stomach
D3A.094	Benign carcinoid tumor of the foregut, unspecified
D3A.095	Benign carcinoid tumor of the midgut, unspecified
D3A.096	Benign carcinoid tumor of the hindgut, unspecified
D3A.098	Benign carcinoid tumors of other sites
E16.1	Other hypoglycemia
E16.3	Increased secretion of glucagon
E16.4	Increased secretion of gastrin
E16.8	Other specified disorders of pancreatic internal secretion
E22.0	Acromegaly and pituitary gigantism
E24.8	Other Cushing's syndrome
E34.0	Carcinoid syndrome
E34.4	Constitutional tall stature
Z85.020	Personal history of malignant carcinoid tumor of stomach
Z85.030	Personal history of malignant carcinoid tumor of large intestine
Z85.040	Personal history of malignant carcinoid tumor of rectum
Z85.060	Personal history of malignant carcinoid tumor of small intestine
Z85.07	Personal history of malignant neoplasm of pancreas
Z85.110	Personal history of malignant carcinoid tumor of bronchus and lung
Z85.230	Personal history of malignant carcinoid tumor of thymus
Z85.858	Personal history of malignant neoplasm of other endocrine glands

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC