Medical Policy Bulletin

Title:
Lanreotide (Somatuline® Depot)
Policy #:
MA08.090h

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.

MEDICALLY NECESSARY

Lanreotide (Somatuline® Depot) is considered medically necessary and, therefore, covered in individuals with the following conditions when the corresponding criteria are met:

ACROMEGALY

- For the long-term treatment of individuals with acromegaly who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.

NEUROENDOCRINE AND ADRENAL TUMORS
Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)

- For the treatment of unresectable, well- or moderately differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.

Neuroendocrine Tumors of the Gastrointestinal Tract (Well-Differentiated Grade 1/2), Lung and Thymus (Carcinoid Tumors)

- For symptom and/or tumor control of recurrent, locoregional advanced disease and/or distant metastases* of the gastrointestinal tract
    - As a single agent if surgical cytoreduction of metastases not possible and low tumor burden
    - As a single agent for disease progression (if not already receiving) following resection of primary, regional lymph nodes plus metastases

    - As a single agent for disease progression (if not already receiving) following resection of primary tumor if symptomatic and/or following observation if surgical cytoreduction of metastases not possible and low tumor burden
    - As a single agent or in combination with alternative front-line therapy if surgical cytoreduction of metastases not possible and clinically significant tumor burden (National Comprehensive Cancer Network [NCCN] preferred)
    - As subsequent therapy a single agent or in combination with subsequent therapy options for clinically significant disease progression (NCCN preferred)
    - At above label dosing after clinical, symptomatic, or radiographic progression (if somatostatin receptors [SSTR]-positive) on standard doses
- For symptom and/or tumor control of recurrent and/or locoregional unresectable lung/thymic disease* if somatostatin receptor positive and/or hormonal symptoms
    - As first-line therapy
    - As subsequent therapy (as alternate first-line therapy) if progression on first-line therapy
- For symptom and/or tumor control of recurrent and/or distant metastatic lung/thymic disease* if somatostatin receptor positive and/or hormonal symptoms
    - As first-line therapy (preferred if clinically significant tumor burden and low grade [typical carcinoid], evidence of disease progression, intermediate grade [atypical carcinoid], or symptomatic)
    - As subsequent therapy (as alternate first-line therapy) if progression on first-line therapy if clinically significant tumor burden and low grade (typical carcinoid), evidence of disease progression, intermediate grade (atypical carcinoid), or symptomatic (NCCN preferred)

NCCN note: *If clinically significant disease progression, treatment with lanreotide (Somatuline® Depot) should be discontinued for nonfunctional tumors and continued in individuals with functional tumors and may be used in combination with any of the subsequent options.

- For symptom control of multiple lung nodules or tumorlets and evidence of diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) as first-line therapy if chronic cough/dyspnea is not responsive to inhalers or conventional treatment
- For symptom control of carcinoid syndrome
    - As a single agent
    - In combination with telotristat for diarrhea due to poorly controlled carcinoid syndrome
    - In combination with other systemic therapy options (based on disease site) with or without telotristat for persistent symptoms (i.e., flushing, diarrhea) due to poorly controlled carcinoid syndrome
- Treatment of carcinoid syndrome for any of the following regimens:
    - As a single agent
    - In combination with telotristat for persistent diarrhea due to poorly controlled carcinoid syndrome
    - In combination with other systemic therapy options (based on disease site) with or without telotristat for persistent symptoms (i.e., flushing, diarrhea) due to poorly controlled carcinoid syndrome

Neuroendocrine and Adrenal Tumors - Well-Differentiated Grade 3 Neuroendocrine Tumors

- For the treatment and/or tumor control of SSTR-positive (if SSTR-positive and/or hormonal symptoms) for unresectable locally advanced/metastatic disease with favorable biology (e.g., relatively low Ki-67 [<55%], slow growing, positive SSR-based PET imaging) at standard dose

Pheochromocytoma/Paraganglioma

- Treatment for secreting tumors for hormone excess and symptom control of locally unresectable disease or distant metastases (if SSTR-positive)

Tumors of the Pancreas (Well-Differentiated Grade 1/2)

- Management of symptoms and/or tumor control of locoregional disease with any of the following indications:
    - Gastrinoma (usually duodenal or head of the pancreas)
    - Insulinoma only if tumor expresses somatostatin receptors
    - Glucagonoma (usually tail)
    - VIPoma

- As NCCN-preferred regimen for symptom and/or tumor control* in individuals** with recurrent or locoregional advanced disease and/or distant metastatic disease if SSTR-positive with any of the following indications:

    - As a single agent for asymptomatic, low tumor burden and stable disease
    - As a single agent for symptomatic, clinically significant tumor burden, or clinically significant progression (if not already receiving)
    - In combination with alternative front-line therapy for symptomatic, clinically significant tumor burden, or clinically significant progression
- For symptom and/or tumor control as subsequent therapy at above label dosing after clinical, symptomatic or radiographic progression on standard doses (if SSTR-positive)

NCCN note: *If clinically significant disease progression, treatment with lanreotide (Somatuline® Depot) should be discontinued for nonfunctional tumors and continued in individuals with functional tumors and may be used in combination with any of the subsequent options.

NCCN note: **For individuals with insulinoma, lanreotide (Somatuline® Depot) should be used only if SSTR-based imaging is positive.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for lanreotide (Somatuline® Depot) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Guidelines

There is no Medicare coverage determination addressing lanreotide (Somatuline® Depot); therefore, the Company policy is applicable.

Lanreotide (Somatuline® Depot) is administered via deep subcutaneous injection.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, lanreotide (Somatuline® Depot) is covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Lanreotide (Somatuline® Depot) was approved by the FDA on August 30, 2007, for the long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy.

Lanreotide (Somatuline® Depot) was approved by the FDA on December 16, 2014, for the treatment of individuals with unresectable, well- or moderately differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors to improve progression-free survival.

Description

Somatostatin is a naturally occurring hormone that has many biological actions because its receptors are found throughout the entire body. Some actions of somatostatin include inhibiting the secretion of growth hormones (GH), prolactin, glucagon, and insulin. Because somatostatin has a short half-life and targets many different hormones,

somatostatin analogues were created (e.g., lanreotide [Somatuline® Depot]). Somatostatin analogues have a long half-life so they can be dosed less often, as well as greater inhibitory selectivity of GH secretion over insulin secretion.

Lanreotide (Somatuline® Depot) is indicated for the long-term treatment of acromegaly, a rare condition characterized by abnormal enlargement of bones in the extremities and head, as well as thickening of soft tissues, such as the heart, lips, and tongue. Acromegaly occurs when the pituitary gland produces too much GH, which in turn causes excess secretion of insulin-like growth factor-1 (IGF-1). Lanreotide (Somatuline® Depot) suppresses the secretion of GH and IGF-1 in individuals who have had inadequate response to or cannot be treated with other therapies, including surgery or radiotherapy, by binding to somatostatin receptors.

Lanreotide (Somatuline® Depot) is also indicated for the treatment of unresectable, well- or moderately differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors. Data have shown that lanreotide (Somatuline® Depot) exhibits antiproliferative effects on these tumors, and improves progression-free survival. Neuroendocrine tumors are a heterogeneous group of neoplasms that arise from neuroendocrine cells and their precursors located throughout the body. Individuals with metastases from neuroendocrine tumors often become symptomatic due to hormone hypersecretion rather than tumor bulk. Lanreotide (Somatuline® Depot) is highly effective in controlling the symptoms associated with neuroendocrine tumors, such as flushing and diarrhea.

CLINICAL STUDIES

ACROMEGALY
The efficacy of lanreotide (Somatuline® Depot) on reducing growth hormone and IGF-1 was evaluated in two trials. The first was a three-phase trial that included a 4-week, double-blind, placebo-controlled phase; a 16-week, single-blind, fixed-dose phase; and a 32-week open-label dose titration phase. A total of 107 individuals completed the placebo-controlled phase, 105 completed the fixed-dose phase, and 99 completed the dose-titration phase. In the first (double-blind) phase of the trial, 52 of 83 (63%) of the lanreotide (Somatuline® Depot)–treated individuals had greater than 50% decrease in mean GH from baseline to week four, compared to 0 in the placebo group. In the fixed-dose phase, 72% of the 107 lanreotide (Somatuline® Depot)–treated individuals had a decrease from baseline in mean GH of greater than 50%. This efficacy was maintained for the duration of the trial.

The second trial was a 48-week, open-label, uncontrolled, multicenter study that enrolled individuals with an IGF-1 level equal to or greater than 1.3 times the upper limit of normal. This trial began with a 4-month fixed-dose phase in which individuals received four deep subcutaneous injections of lanreotide (Somatuline® Depot) at 4-week intervals. This was followed by a dose-titration phase in which the dose of lanreotide (Somatuline® Depot) was adjusted based on GH and IGF-1 levels. Sixty-three individuals started the fixed-dose phase and 57 completed 48 weeks of treatment. At the completion (48 weeks) of the trial, 43% (27/63) achieved normal age-adjusted IGF-1 levels, 38% (24/63) of individuals achieved both normal IGF-1 levels and GH levels less than or equal to 2.5 ng/mL, and 27% (17/63) had both normal IGF-1 levels and GH levels less than 1 ng/mL.

GASTROENTEROPANCREATIC NEUROENDOCRINE TUMORS
Efficacy of lanreotide (Somatuline® Depot) in the treatment of gastroenteropancreatic neuroendocrine tumors was evaluated in a multicenter, randomized, double-blind, placebo-controlled trial of 204 individuals. Individuals received either lanreotide (Somatuline® Depot) or placebo every 4 weeks until disease progression, unacceptable toxicity, or a maximum of 96 weeks. Primary outcome was progression-free survival. Individuals in the lanreotide (Somatuline® Depot) arm had statistically significant improvement in progression-free survival compared to those in the placebo arm. Median progression-free survival was not reached in the lanreotide (Somatuline® Depot) group, and was 16.6 months in the placebo group.

OFF-LABEL INDICATION

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)
N/A

ICD - 10 Procedure Code Number(s)
N/A

ICD - 10 Diagnosis Code Number(s)
N/A

HCPCS Level II Code Number(s)
J1930 Injection, lanreotide, 1 mg
J1932 Injection, lanreotide, (cipla), 1 mg

Revenue Code Number(s)
N/A

Policy History

Revisions From MA08.090h:

12/15/2025	This version of the policy will become effective 12/15/2025. This policy was updated to communicate the coverage position changes for neuroendocrine and adrenal tumors (pheochromocytoma/paraganglioma, neuroendocrine tumors of the gastrointestinal tract, lung and thymus [carcinoid tumors], neuroendocrine tumors of the pancreas) in accordance with the National Comprehensive Cancer Network (NCCN). All of the ICD-10 CM codes have been removed from this policy, since they are informational. Report the most appropriate diagnosis code in support of medically necessary criteria as listed in the policy. Attachment A was removed from the policy.

Revisions From MA08.090g:

12/16/2024	This policy has been identified for the ICD-10 code update, effective 12/16/2024. The following ICD-10 code has been **removed** from Attachment A of this policy: • E34.0 Carcinoid syndrome The following ICD-10 codes have been **added** to Attachment A of this policy: • E34.00 Carcinoid syndrome, unspecified • E34.01 Carcinoid heart syndrome • E34.09 Other carcinoid syndrome

Revisions From MA08.090f

05/07/2024	This version of the policy will become effective 05/07/2024. This policy was updated to communicate the coverage position changes for neuroendocrine tumors of the gastrointestinal tract, lung and thymus [carcinoid tumors], neuroendocrine tumors of the pancreas, Pheochromocytoma/Paraganglioma in accordance with the National Comprehensive Cancer Network (NCCN). The following ICD-10 codes have been added to the coding policy: 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

Revisions From MA08.090e

10/01/2022	This version of the policy will become effective 10/01/2022 Inclusion of a policy in a Code Update memo does not imply that a full review of the policy was completed at this time. The following HCPCS code has been **added** to this policy: J1932 Injection, lanreotide (cipla), 1 mg

Revisions From MA08.090d:

06/20/2022	This version of the policy will become effective 06/20/2022 This policy was updated to communicate the coverage position changes for neuroendocrine and adrenal tumors (pheochromocytoma/paraganglioma, neuroendocrine tumors of the gastrointestinal tract, lung and thymus [carcinoid tumors], neuroendocrine tumors of the pancreas) in accordance with the National Comprehensive Cancer Network (NCCN). The following ICD- 10 codes have been added to the policy: C25.0 Malignant neoplasm of head of pancreas C25.1 Malignant neoplasm of body of pancreas C25.2 Malignant neoplasm of body of pancreas C25.3 Malignant neoplasm of body of pancreatic duct C25.7 Malignant neoplasm of other parts of pancreas C25.8 Malignant neoplasm of overlapping sites pancreas C25.9 Malignant neoplasm of pancreas, unspecified C26.0 Malignant neoplasm of intestinal tract, part unspecified C26.9 Malignant neoplasm of ill-defined sites within the digestives system D37.8- Neoplasm of uncertain behavior of other specified digestive organs D49.0- Neoplasm of unspecified behavior of digestive system D37.8- Neoplasm of uncertain behavior of other specified digestive organs D49.0- Neoplasm of unspecified behavior of digestive system

Revisions From MA08.090c:

03/01/2021	This version of the policy will become effective 03/01/2021 This policy was updated to communicate the coverage position changes for neuroendocrine and adrenal tumors (pheochromocytoma/paraganglioma, neuroendocrine tumors of the gastrointestinal tract, lung and thymus [carcinoid tumors], neuroendocrine tumors of the pancreas) in accordance with the National Comprehensive Cancer Network (NCCN).

Revisions From MA08.090b:

12/30/2019.	This version of the policy will become effective 12/30/2019. This policy was updated to communicate the coverage position changes for neuroendocrine and adrenal tumors (pheochromocytoma/paraganglioma, neuroendocrine tumors of the gastrointestinal tract, lung, and thymus [carcinoid tumors], neuroendocrine tumors of the pancreas) in accordance with the National Comprehensive Cancer Network (NCCN).

Revisions From MA08.090a:

11/19/2018	This version of the policy will become effective 11/19/2018. This policy has been updated to communicate changes based on National Comprehensive Cancer Network (NCCN) compendium. Included criteria for neuroendocrine tumors

Revisions From MA08.090:

01/01/2018	This version of the policy will become effective 01/01/2018. This new policy has been developed to communicate the Company's coverage criteria for lanreotide (Somatuline® Depot).

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