Somatuline Depot (lanreotide) and Lanreotide Injection

Policy Number: MC/PC 041
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Instructions for Use

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Related Policies

- Oncology Medication Clinical Coverage

Coverage Rationale

This policy is applicable for lanreotide for injection for non-oncology indications only. Please see the 'Oncology Medication Clinical Coverage' Policy for oncology indications.

Acromegaly

For initial coverage of Somatuline Depot (lanreotide) and Lanreotide Injection for acromegaly, all of the following will be required:

- Diagnosis of acromegaly **and**
- One of the following:
  - Inadequate response to surgery or radiotherapy **or**
  - Not a candidate for surgery or radiotherapy **and**
- Prescribed by or in consultation with an endocrinologist or neurosurgeon.

For reauthorization coverage of Somatuline Depot (lanreotide) and Lanreotide Injection for acromegaly, the following will be required:

- Patient demonstrates positive clinical response to therapy, such as a reduction or normalization of IGF-1/GH level for same age and gender

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan

document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1930	Injection, lanreotide, 1 mg
J1932	Injection, lanreotide, (cipla), 1 mg

ICD-10 Code	Description
E22.0	Acromegaly and pituitary gigantism

Background

Acromegaly is a rare and serious systemic disease caused by hypersecretion of GH, most often due to pituitary adenoma. This hypersecretion induces the synthesis of insulin like growth factor-1 (IGF-1) causing metabolic dysfunction and significant comorbidities (ie, cardiovascular disease, diabetes mellitus type 2, carpal tunnel syndrome and sleep apnea) (Gomes-Porras et al 2020, Melmed and Katznelson 2021). Three SSAs (octreotide, lanreotide, and pasireotide) and the GH receptor antagonist (pegvisomant) are available for the treatment of acromegaly. Dopamine agonists (eg, cabergoline, bromocriptine) are also used to achieve disease control. Lanreotide is an inhibitor of various endocrine, neuroendocrine, exocrine, and paracrine functions. In acromegalic patients, lanreotide reduces growth hormone and IGF-1 levels.

Clinical Evidence

Acromegaly

A Phase 3, global, open-label (OL), non-inferiority trial assessed the maintenance of biochemical response and symptomatic control with oral octreotide vs injectable SSA (eg, long-acting octreotide or lanreotide depot) in 218 patients with acromegaly who previously tolerated and responded to both treatments. The primary outcome was the non-inferiority assessment (margin -20 percentage points) of the proportion of patients who were biochemically controlled throughout the 62-week RCT phase. A patient was considered biochemically controlled if IGF-1 was < 1.3 × ULN. All eligible patients (N = 146) entered a 26-week run-in phase, all of whom received oral octreotide. Eligibility for the RCT was the completion of the run-in phase as a biochemical responder (IGF-I < 1.3 × ULN and mean integrated GH < 2.5 ng/mL at week 24) and investigator assessment of acromegaly being adequately controlled. Patients in the RCT phase (N = 92) were randomly assigned 3:2 to oral octreotide or injectable SSA at the same dose and interval as before enrollment. The lower bound of the 2-sided 95% CI for the adjusted difference in proportions between the 2 treatment groups achieved the prespecified non-inferiority criterion of -20% (95% CI, -19.9 to 0.5). The most common adverse effects (AEs) in both groups were gastrointestinal (GI) (Flesuriu et al 2022[a])

A network meta-analysis of 7 RCTs in 767 patients with acromegaly assessed and compared the efficacy and safety of lanreotide sustained release (SR; not available in the United States), lanreotide depot, octreotide LAR, pasireotide LAR, pegvisomant, and placebo, with the primary efficacy outcome of the number of patients who achieved IGF-1 control (Leonart et al 2018). For the number of patients achieving IGF-1, statistically significant differences were observed between pegvisomant and placebo (OR, 0.06; 95% credible interval [CrI], 0.00 to 0.55) and between lanreotide depot and placebo (OR, 0.09; 95% CrI, 0.01 to 0.88). For the probability ranking of IGF-1 control, the surface under the cumulative ranking curve (SUCRA) analysis indicated that pegvisomant and pasireotide LAR had the highest probabilities of being the best treatment option (73.4% and 73.0%, respectively), whereas placebo was the worst alternative (4.6%). A (SUCRA) ranking estimates the probability of a treatment being ranked first, second, third, etc.; SUCRA would be 100% if treatment always ranks first and 0% if treatment always ranks last. Regarding safety, most trials reported injection site reactions and GI disorders, usually of mild to moderate intensity. Glucose metabolism disorders leading to treatment

discontinuation were reported for pasireotide LAR; however, these types of AEs were also observed with other SSA treatments.

A 12-month, randomized, crossover study of 10 patients with acromegaly comparing octreotide LAR to lanreotide depot showed that both agents were almost equally efficient in obtaining clinical and biochemical control of acromegaly, and that a change from lanreotide depot to octreotide LAR or vice versa may be beneficial in some patients with treatment failure or AEs (Andries et al 2008).

Clinical Guidelines

Acromegaly
The Endocrine Society clinical practice guidelines for acromegaly include the following recommendations (Katznelson et al 2014):

- Because of the variable nature of acromegaly, an individualized treatment strategy is necessary.
    - Goals of treatment are biochemical normalization, reduction of mortality risk, attenuation of symptoms, control of tumor mass, and maintenance of pituitary function.
- TSS is the primary therapy in most patients, and medical therapy is recommended in a patient with persistent disease following surgery. Radiotherapy is suggested in the setting of residual tumor mass following surgery, and if medical therapy is unavailable, unsuccessful, or not tolerated.
- In patients with significant disease, use of either an SSA or pegvisomant as the initial adjuvant medical therapy is suggested.
    - SSAs: Octreotide LAR and lanreotide depot are equally effective; these agents achieve IGF-1 normalization in about 17 to 35% of patients and reduce tumor volume > 50% in the majority of patients.
    - Pegvisomant exhibits a favorable benefit in glycemic control, and it may be useful for patients with diabetes mellitus. Dose-dependent normalization of IGF-1 levels was achieved in up to 95% of patients in pivotal trials and maintained in 63% of patients after 5 years of pegvisomant therapy in a published surveillance study of 1288 patients.
    - Combination therapy: May improve efficacy, reduce AEs associated with individual medications, decrease the frequency of injections and total drug dose, and potentially offer a cost benefit and improved compliance during long-term treatment. Addition of pegvisomant or cabergoline in a patient with inadequate response to an SSA is suggested. The combination of pegvisomant and cabergoline (dopamine receptor agonist) might be useful in some patients.
- The guidelines have not been updated to include Signifor LAR (pasireotide) injection or Mycapssa (octreotide) capsules.

The 2020 Pituitary Society update to acromegaly management guidelines include the following recommendations (Fleseriu et al 2021[b]):

- Injectable somatostatin receptor ligand (SRL)
    - Older age, female sex, lower IGF-I levels, and tumor T2 MRI hypo intensity at baseline predict more favorable long-term biochemical responses to primary lanreotide 120 mg therapy every 4 weeks. (MQ, SR)
    - Recent studies confirm that extended-dosing intervals (>4 weeks) for 120 mg lanreotide may be effective among selected patients previously controlled with long-acting SRLs. (LQ, DR)
    - Several studies confirm efficacy of pasireotide LAR for some patients uncontrolled on lanreotide or octreotide LAR. However, rates of treatment-induced hyperglycemia and DM are high, requiring careful monitoring for glycemic side effects. (HQ, SR)
- Pegvisomant
    - Ten-year follow-up from ACROSTUDY shows a 73% biochemical control rate with very low rates of transient elevated transaminases and 6.8% exhibiting tumor growth visible on MRI. (HQ, SR)

    - Pegvisomant use in patients with DM improves glucose metabolism independent of IGF-I control, but does not affect glycemic endpoints in patients without DM. (MQ, SR)
    - Patients with DM and those with a higher BMI require higher doses of pegvisomant and more rapid up-titration to achieve IGF-I normalization. (MQ, SR)
- Combination therapy with SRL+pegvisomant
    - Low-dose octreotide LAR or lanreotide plus weekly pegvisomant is a cost-effective and efficacious option for patients requiring combination therapy. (HQ, SR)
    - Combination of pasireotide plus pegvisomant can yield biochemical control rates exceeding 70% even when pegvisomant doses are kept low.
    - However, the addition of pegvisomant does not ameliorate the high rates of pasireotide-induced hyperglycemia. (MQ, SR)
    - Patient selection for combination pasireotide plus pegvisomant should be carefully considered. (LQ, DR)
- Oral octreotide capsules (OOC)
    - OOC are suitable for patients who have demonstrated complete or partial biochemical response on injectable octreotide or lanreotide. (HQ, SR)
        - Rationale: As octreotide and lanreotide have similar efficacy, patients who have responded to these injectable agents are candidates for OOC therapy, and results of the OPTIMAL study demonstrate that biochemically controlled patients (IGF-I≤1.0×ULN) on stable doses of injectable octreotide or lanreotide maintain response to OOC [4]. There are no data regarding efficacy of switching patients from pasireotide LAR to OOC. There are no data on the use of OOC as primary medical therapy in SRL-naïve patients. However, it is reasonable to expect that patients who respond to injectable octreotide LAR or lanreotide in this setting would also respond to OOC
    - Due to a lack of available data, OOC is not currently recommended for patients who have tumor characteristics predictive of octreotide resistance. (MQ, SR) Rationale: Tumor characteristics associated with octreotide and lanreotide resistance (e.g., MRI T2 hyperintensity, sparsely granulated tumors) are presumed to also predict resistance to OOC

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Somatuline depot is a somatostatin analog indicated for:
- the long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy.
- the treatment of adult patients with unresectable, well- or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.
- the treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

Lanreotide Injection is a somatostatin analog indicated for:
- The long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy.
- The treatment of adult patients with unresectable, well- or moderately- differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.

References

1. Andries M, Glintborg D, Kvistborg A, et al. A 12-month randomized crossover study on the effects of lanreotide autogel and octreotide long-acting repeatable on GH and IGF-1 in patients with acromegaly. *Clin Endocrinol.* 2008;68:473-480.
2. Fleseriu M, Dreval A, Bondar I, et al. A Pituitary Society update to acromegaly management guidelines. *Pituitary* 2021[b]; 24:1–13. doi:10.1007/s11102-020-01091-7
3. Fleseriu M, Biller B, Freda P, et al. Maintenance of response to oral octreotide compared with injectable somatostatin receptor ligands in patients with acromegaly: a phase 3, multicentre, randomised controlled trial. Lancet Diabetes Endocrinol. 2022[a];10(2):102-111.
4. Katznelson L, Laws ER Jr, Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99(11):3933-3951. doi:10.1210/jc.2014-2700.
5. Leonart LP, Ferreira VL, Tonin FS, Fernandez-Llimos F, Pontarolo R. Medical treatments for acromegaly: A systematic review and network meta-analysis. Value Health. 2018;21(7):874-880.
6. Gomes-Porras M, Cardenas-Salas J, Alvarez-Escola C. Somatostatin anologs in clinical practice: a review. Int J Mol Sci. 2020;21(5):1682.
7. LANREOTIDE ACETATE- lanreotide acetate injection [package insert], Warren, NJ: Cipla USA, Inc.; July 2024.
8. Melmed S, Katznelson L. Diagnosis of acromegaly. UpToDate Web site. https://www.uptodate.com. Updated December 3, 2021. Accessed August 21, 2024.
9. Somatuline Depot [package insert], Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; July 2024.

Policy History/Revision Information

Date	Summary of Changes
12/13/2023	Approved by OptumRx P&T Committee
10/16/2024	Annual Review. References updated. No clinical content changed.

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Archived Policy Versions (Internal Only)

Effective Date	Policy Number	Policy Title
mm/dd/yyyy – mm/dd/yyyy	######	Title of Policy Hyperlinked to KL or Other Internal Location

Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1-800-332-6501 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).

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