Sandostatin (octreotide acetate) LAR Depot Injection (Non-Oncology Indications)

Policy Number: MC/PC 038
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Instructions for Use

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Related Policies

- Oncology Medication Clinical Coverage

Coverage Rationale

Acromegaly

For initial coverage of Sandostatin (octreotide acetate) LAR Depot Injection for acromegaly the following will be required:

- Diagnosis of acromegaly **and**
- One of the following:
  - Inadequate response to one of the following:
    - Surgery
    - Pituitary irradiation **or**
  - Not a candidate for surgical resection or pituitary irradiation **and**
- Trial and failure, contraindication, or intolerance to a dopamine agonist (e.g., bromocriptine or cabergoline) at maximally tolerated doses.
- Patient has had a trial of short-acting generic octreotide and responded to and tolerated therapy.

For reauthorization coverage of Sandostatin (octreotide acetate) LAR Depot Injection for acromegaly, the following will be required:

- Presence of positive clinical response to therapy (e.g., reduction or normalization of IGF-1/GH level for same age and sex, reduction in tumor size)

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
J2353	Injection, Octreotide, depot form for intramuscular injection, 1mg

ICD-10 Code	Description
E22.0	Acromegaly and pituitary gigantism
K52.1	Toxic gastroenteritis and colitis
T38.895A	Adverse effect of other hormones and synthetic substitutes, initial encounter
T38.895D	Adverse effect of other hormones and synthetic substitutes, subsequent encounter
T38.895S	Adverse effect of other hormones and synthetic substitutes, sequela
T43.215A	Adverse effect of selective serotonin and norepinephrine reuptake inhibitors, initial encounter
T43.215D	Adverse effect of selective serotonin and norepinephrine reuptake inhibitors, subsequent encounter
T43.215S	Adverse effect of selective serotonin and norepinephrine reuptake inhibitors, sequela
T43.225A	Adverse effect of selective serotonin reuptake inhibitors, initial encounter
T43.225D	Adverse effect of selective serotonin reuptake inhibitors, subsequent encounter
T43.225S	Adverse effect of selective serotonin reuptake inhibitors, sequela
T43.641A	Poisoning by ecstasy, accidental (unintentional), initial encounter
T43.641D	Poisoning by ecstasy, accidental (unintentional), subsequent encounter
T43.641S	Poisoning by ecstasy, accidental (unintentional), sequela
T43.642A	Poisoning by ecstasy, intentional self-harm, initial encounter
T43.642D	Poisoning by ecstasy, intentional self-harm, subsequent encounter
T43.642S	Poisoning by ecstasy, intentional self-harm, sequela
T43.643A	Poisoning by ecstasy, assault, initial encounter
T43.643D	Poisoning by ecstasy, assault, subsequent encounter
T43.643S	Poisoning by ecstasy, assault, sequela
T43.644A	Poisoning by ecstasy, undetermined, initial encounter
T43.644D	Poisoning by ecstasy, undetermined, subsequent encounter
T43.644S	Poisoning by ecstasy, undetermined, sequela
T50.995A	Adverse effect of other drugs, medicaments and biological substances, initial encounter
T50.995D	Adverse effect of other drugs, medicaments and biological substances, subsequent encounter
T50.995S	Adverse effect of other drugs, medicaments and biological substances, sequela
R79.89	Other specified abnormal findings of blood chemistry
R94.7	Abnormal results of other endocrine function studies
K52.89	Other specified noninfective gastroenteritis and colitis
R19.7	Diarrhea, unspecified
I85.00	Esophageal varices without bleeding
I85.01	Esophageal varices with bleeding

ICD-10 Code	Description
I85.10	Secondary esophageal varices without bleeding
I85.11	Secondary esophageal varices with bleeding
K76.7	Hepatorenal syndrome
K91.82	Postprocedural hepatic failure
K91.83	Postprocedural hepatorenal syndrome
O90.4	Postpartum acute kidney failure
E13.641	Other specified diabetes mellitus with hypoglycemia with coma
E13.649	Other specified diabetes mellitus with hypoglycemia without coma

Background

Somatostatin is a cyclic polypeptide and a main inhibitor of a broad range of hormones such as growth hormone (GH), prolactin, gastric inhibitory peptide, gastrin, glucagon, insulin, and pancreatic polypeptide. Somatostatin analogs (SSAs) are a therapeutic option for the treatment of many conditions including somatotropinomas (i.e., acromegaly), neuroendocrine tumors (NETs) (i.e., carcinoid syndrome and vasoactive intestinal peptide tumors [VIPomas]), and Cushing's syndrome (CS) (Gomes-Porras et al 2020). Octreotide exerts pharmacologic actions similar to the natural hormone and is an even more potent inhibitor of growth hormone (GH), glucagon, and insulin than somatostatin. Like somatostatin, it also suppresses luteinizing hormone response to gonadotropin releasing hormone, decreases splanchnic blood flow, and inhibits release of serotonin, gastrin, VIP, secretin, and pancreatic polypeptide. Octreotide LAR is a long-acting dosage form consisting of microspheres of the biodegradable glucose star polymer, D,L-lactic and glycolic acids copolymer, containing octreotide. It maintains all the clinical and pharmacological characteristics of octreotide with the added feature of slow release of octreotide from the site of injection, reducing the need for frequent administration.

Acromegaly is a rare and serious systemic disease caused by hypersecretion of growth hormone (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 (i.e., cardiovascular disease, diabetes mellitus type 2, carpal tunnel syndrome and sleep apnea) (Gomes-Porras et al 2020, Melmed and Katznelson 2021). Three somatostatin analogs (SSAs; (octreotide, lanreotide, and pasireotide) and the growth hormone (GH) receptor antagonist (pegvisomant) are available for the treatment of acromegaly. Dopamine agonists (e.g., cabergoline, bromocriptine) are also used to achieve disease control. Acromegaly is considered a rare disease, with an estimated prevalence of 14 to 85 cases per million people worldwide, with an incidence of 1 to 11 cases per million per year across the world (Leonart et al 2018). Due to the variable nature of acromegaly, an individualized multidisciplinary treatment strategy is necessary. Goals of treatment are biochemical normalization, reduction of mortality risk, attenuation of symptoms, control of tumor size and reduction of mass effects, maintenance of pituitary function, and reversal of metabolic abnormalities such as diabetes mellitus (Katznelson et al 2014, Leonart et al 2018, Melmed and Katznelson 2023).

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).

A 12-month, prospective, multicenter, doub, RCT in 358 medically naïve patients with acromegaly demonstrated that the efficacy of pasireotide LAR was superior to octreotide LAR, with 38.6% and 23.6% (p = 0.002) of patients achieving normal IGF-1 levels, respectively. Hyperglycemia-related AEs were more common with pasireotide LAR (57.3 vs 21.7%, respectively) (Colao et al 2014).

PAOLA, a Phase 3, MC, RCT (N = 198) evaluated the efficacy and safety of 2 different doses of pasireotide LAR (40 mg or 60 mg) compared with active control (long-acting octreotide or lanreotide) in patients with inadequately controlled acromegaly. The primary endpoint was number of patients achieving biochemical control, defined as mean GH concentration < 2.5 μ g/L and normal IGF-1 concentration. At 24 weeks, 10 (15%) patients in the pasireotide 40 mg group and 13 (20%) patients in the pasireotide 60 mg group achieved biochemical control, vs 0 patients in the active control group, with absolute differences from the control group of 15.4% (95% CI, 7.6 to 26.5; p = 0.0006) and 20% (95% CI, 11.1 to 31.8; p < 0.0001), respectively (Gadelha et al 2014).

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. Transsphenoidal surgery (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. 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.

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.

SANDOSTATIN LAR DEPOT is indicated in patients in whom initial treatment with Sandostatin Injection has been shown to be effective and tolerated.

Acromegaly
Long-term maintenance therapy in acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy, is not an option. The goal of treatment in acromegaly is to reduce GH and IGF-1 levels to normal.

References

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Policy History/Revision Information

Date	Summary of Changes
9/20/2023	Approved by OptumRx P&T Committee
11/21/2024	Annual Review. Updated criteria in line with PA guideline and updated references.

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).

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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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