



Drug Coverage Policy

Effective Date..... 5/1/2026

Coverage Policy Number IP0165

Policy Title..... Signifor LAR

Somatostatin Analogs – Signifor LAR

- Signifor® LAR (pasireotide intramuscular injection – Recordati Rare Diseases)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see “Coding Information” below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Signifor LAR, a somatostatin analog, is indicated for the following uses:¹

- **Acromegaly**, in patients who have had an inadequate response to surgery and/or for whom surgery is not an option. In vivo studies show that Signifor LAR lowers growth hormone and insulin-like growth factor-1 levels in patients with acromegaly.
- **Cushing's disease**, in patients for whom pituitary surgery is not an option or has not been curative.

Guidelines

The Endocrine Society published clinical practice guidelines for the treatment of Cushing's syndrome in (2015) and Cushing's disease (2021).^{2,3} Recorlev is recognized in the 2021 guidelines for Cushing's disease as investigational; further details regarding this therapy are not discussed. Treatment goals for Cushing's syndrome are to normalize cortisol levels or its action at the receptors to eliminate signs and symptoms of Cushing's syndrome. Best practice adjunctive management include treating co-morbidities associated with hypercortisolism (psychiatric disorders, diabetes, hypertension, hypokalemia, infections, dyslipidemia, osteoporosis, and poor physical fitness). First-line treatment involves resection of the tumor, unless surgery is not possible or is unlikely to meaningfully reduce excess glucocorticoid. Specifically for Cushing's disease, transsphenoidal selective adenomectomy by a surgeon with extensive experience in pituitary surgery is recommended. In patients with ACTH-dependent Cushing's syndrome who underwent noncurative surgery or for whom surgery was not possible, the guidelines advocate several second-line therapies (e.g., repeat transsphenoidal surgery, radiotherapy, medical therapy, and bilateral adrenalectomy). For Cushing's disease, the guidelines recommend all medical therapies as second-line options after transsphenoidal surgery. These involve steroidogenesis inhibitors (ketoconazole, Metopirone[®] [metyrapone capsules], Lysodren[®] [mitotane tablets], etomidate) in patients either with or without radiotherapy/radiosurgery; pituitary-directed medical treatments (cabergoline, Signifor[®] [pasireotide subcutaneous injection]) in patients who are not surgical candidates or who have persistent disease; and Korlym[®] (mifepristone tablets) in patients with diabetes or glucose intolerance who are not surgical candidates or who have persistent disease after transsphenoidal surgery.

The 2025 international Acromegaly Consensus Statement reaffirms somatostatin analogs as the first-line medical therapy for most patients with persistent or non-surgically managed disease, with goals of insulin-like growth factor 1 (IGF-1) normalization, symptom control, and tumor growth prevention.⁴ Injectable octreotide and lanreotide achieve biochemical control in approximately 40% of patients, with dose escalation or increased dosing frequency recommended before switching therapy. Mycapssa[®] (octreotide delayed-release capsules) is considered non-inferior to injectable somatostatin analogs in patients previously controlled on injectables and may be selected based on patient preference and adherence. Signifor LAR provides greater efficacy in some inadequately controlled patients but carries a higher risk of hyperglycemia, and the consensus emphasizes individualized therapy selection and increasing use of combination therapy with Somavert[®] (pegvisomant subcutaneous injection) for partial responders.

The Endocrine Society Clinical Practice Guidelines (2014) recommend medical therapy primarily as adjuvant treatment following surgery, with somatostatin analogs used when surgery is not curative or the patient is a poor surgical candidate.⁵ No preferred somatostatin analog is specified, and Mycapssa is not addressed in the 2014 guidelines. Subsequent updates from the Acromegaly Consensus Group (2020) recommend lanreotide deep subcutaneous injection and octreotide long-acting intramuscular injection as first-line medical therapies for persistent disease after surgery.⁶ These updates also recommend Mycapssa for patients who respond to and tolerate injectable lanreotide or octreotide. Signifor LAR is positioned as a second-line therapy due to its increased risk of hyperglycemia. The Pituitary Society Update to Acromegaly Management Guidelines (2021) recommend a personalized approach to acromegaly medication management, especially for patients who are not surgical candidates or have residual disease.⁷ First-line therapies include somatostatin analogs, with Somavert and cabergoline used for resistant or mild cases.

Mycapssa offers more convenient options, with treatment tailored to biochemical response, tumor features, and patient preferences.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for prescription benefit coverage of Signifor. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Signifor as well as the monitoring required for adverse events and long-term efficacy, approval requires Signifor to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Signifor LAR is considered medically necessary when ONE of the following are met:

FDA-Approved Indications

- 1. Acromegaly.** Approve for 1 year if the patient meets ALL of the following (A, B, C and D):
 - A)** Patient meets ONE of the following (i, ii, or iii):
 - i.** Patient has had an inadequate response to surgery and/or radiotherapy; OR
 - ii.** Patient is NOT an appropriate candidate for surgery and/or radiotherapy; OR
 - iii.** Patient is experiencing negative effects due to tumor size (e.g., optic nerve compression); AND
 - B)** Patient has (or had) a pre-treatment (baseline) insulin-like growth factor-1 (IGF-1) level above the upper limit of normal based on age and gender for the reporting laboratory; AND
Note: Pre-treatment (baseline) refers to the IGF-1 level prior to the initiation of any somatostatin analog (e.g., Mycapssa [octreotide delayed-release capsules], an octreotide acetate injection product [e.g., Bynfezia Pen, Sandostatin {generic}, Sandostatin LAR Depot], Signifor LAR [pasireotide injection], Somatuline Depot [lanreotide injection], dopamine agonist [e.g., cabergoline, bromocriptine], or Somavert [pegvisomant injection]). Reference ranges for IGF-1 vary among laboratories.
 - C)** The medication is prescribed by or in consultation with an endocrinologist.
 - D)** Preferred product criteria are met for the product(s) as listed in the below table(s).

Dosing. Approve up to 60 mg administered intramuscularly no more frequently than every 28 days.

- 2. Cushing's Disease.** Approve for the duration noted if the patient meets ONE of the following (A or B):
 - A) Initial Therapy.** Approve for 4 months of initial therapy if the patient meets ALL of the following (i, and ii,):
 - i.** According to the prescriber, patient is not a candidate for surgery, or surgery has not been curative; AND
Note: For patients with Cushing's disease/syndrome awaiting surgery, see *Other Uses with Supportive Evidence*.
 - ii.** Signifor LAR is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of Cushing's disease.
 - B) Patient is Currently Receiving Signifor LAR/Signifor.** Approve for 1 year of continuation therapy if the patient has responded to Signifor/Signifor LAR, as determined by the prescriber.
Note: An example of patient response is decrease in the mean urinary free cortisol level.

Dosing. Approve up to 40 mg administered intramuscularly no more frequently than once every 28 days.

Other Uses with Supportive Evidence

- 3. Endogenous Cushing’s Syndrome.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- A)** Patient is ≥ 18 years of age; AND
 - B)** Patient meets ONE of the following (i, ii, or iii)
 - i.** According to the prescriber, the patient is not a candidate for surgery or surgery has not been curative; OR
 - ii.** Patient is awaiting surgery for **endogenous Cushing’s Syndrome**; OR
 - iii.** Patient is awaiting therapeutic response after radiotherapy for **endogenous Cushing’s Syndrome**; AND
 - C)** The medication is prescribed by or in consultation with an endocrinologist or a physician who specialized in the treatment of Cushing’s syndrome.

Dosing. Approve up to 40 mg administered intramuscularly no more frequently than once every 28 days.

Employer Plans:

Product	Criteria
Signifor LAR (pasireotide IM injection)	For a diagnosis of Acromegaly, patient has tried ONE of octreotide ER injectable suspension (Sandostatin LAR Depot, generic), Somatuline Depot or lanreotide subcutaneous injection [may require prior authorization]. Note: If requesting a Cipla lanreotide product, the preferred product is J1930, NDC 69097- 0906 -67

Conditions Not Covered

Signifor LAR for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

Coding Information

- 1) This list of codes may not be all-inclusive.
- 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J2502	Injection, pasireotide long acting, 1 mg

References

1. Signifor® LAR subcutaneous injection [prescribing information]. Lebanon, NJ: Recordati Rare Diseases; July 2024.

2. Nieman LK, Biller BM, Findling JW. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2015;100(8):2807-2831.
3. Fleseriu M, Auchus R, Bancos I, et al. Consensus on diagnosis and management of Cushing's disease: a guideline update. *Lancet Diabetes Endocrinol.* 2021;9(12):847-875.
4. Melmed S, di Filippo L, Fleseriu M, et al. Consensus on acromegaly therapeutic outcomes: an update. *Nat Rev Endocrinol.* 2025;21(11):718-737.
5. Katznelson L, Laws ER Jr, Melmed S, et al; Endocrine Society. Acromegaly: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2014;99:3933-3951.
6. Giustina A, Barkhoudarian G, Beckers A, et al. Multidisciplinary management of acromegaly: A consensus. *Rev Endocr Meta Disord.* 2020;21(4):667-678.
7. Fleseriu M, Biller, BMK, Freda PU, et al. A Pituitary Society update to acromegaly management guidelines. *Pituitary.* 2021; 24:1-13.

Revision Details

Summary of Changes	Review Date	Effective Date
<p>Updated coverage policy title from <i>Pasireotide Long-Acting to Somatostatin Analogs – Signifor LAR</i>.</p> <p>Endogenous Cushing's Syndrome: Added this condition and criteria for approval under <i>Other Uses with Supportive Evidence</i>.</p> <p>Endogenous Cushing's Syndrome – Patient Awaiting Surgery: Removed this condition from the policy and is now addressed under Endogenous Cushing's Syndrome.</p> <p>Endogenous Cushing's Syndrome – Patient Awaiting Therapeutic Response After Radiotherapy: Removed this condition from the policy and is now addressed under Endogenous Cushing's Syndrome.</p> <p>Endogenous Cushing's Syndrome. Updated initial authorization duration from 4 months to 1 year</p> <p>Endogenous Cushing's Syndrome – Individual Awaiting Surgery: Removed from authorization duration: 'if individual is still awaiting surgery, then reauthorize for 4 months</p> <p>Cushing Disease: Added 'Patient is Currently Receiving Signifor/Signifor LAR' criteria</p>	5/23/2024	8/1/2024
No criteria changes.	5/8/2025	7/15/2025
Preferred Product Table.	2/5/2026	4/1/2026

<p>Updated from "For a diagnosis of Acromegaly only. Patient has tried Somatuline Depot (lanreotide acetate) injection." to "For a diagnosis of Acromegaly, patient has tried ONE of octreotide ER injectable suspension (Sandostatin LAR Depot, generic), Somatuline Depot or lanreotide subcutaneous injection [may require prior authorization]. Note: If requesting a Cipla lanreotide product, the preferred product is J1930, NDC 69097-0906-67"</p>		
<p>No criteria changes</p>	<p>4/16/2026</p>	<p>5/1/2026</p>

The policy effective date is in force until updated or retired.

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