CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Somatostatin Analogs – Signifor LAR Utilization Management Medical Policy
- Signifor® LAR (pasireotide intramuscular injection – Recordati Rare Diseases)

REVIEW DATE: 04/08/2026

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 adenectomy 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.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Signifor LAR. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Signifor LAR as well as the monitoring required for adverse events and long-term efficacy, approval requires Signifor LAR to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Signifor LAR is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Acromegaly. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

- **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.

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; OR

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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Signifor LAR is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	**Endogenous Cushing's Syndrome:** This condition was added under other uses with supportive evidence. **Endogenous Cushing's Syndrome – Patient Awaiting Surgery:** This condition was removed from the policy (now addressed under Endogenous Cushing's Syndrome). **Endogenous Cushing's Syndrome – Patient Awaiting Therapeutic Response After Radiotherapy:** This condition was removed from the policy (now addressed under Endogenous Cushing's Syndrome).	04/19/2024
Annual Revision	No criteria changes.	04/23/2025
Annual Revision	No criteria changes.	04/08/2026