PRIOR AUTHORIZATION POLICY

POLICY: Somatostatin Analogs – Signifor LAR Prior Authorization Policy
- Signifor® LAR (pasireotide intramuscular injection – Recordati Rare Diseases)

REVIEW DATE: 04/19/2024

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.

Disease Overview

Cushing's syndrome refers to the general state of excessive levels of cortisol (hypercortisolism) in the blood.[2,3] Hypercortisolism can occur for reasons that are either endogenous or exogenous in nature (e.g., Cushing's disease, cortisol-containing medications, adrenal gland tumor, certain cancers). Cushing's disease (hypercortisolism caused by pituitary adenomas) is the most common type of adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome. Treatment for Cushing's syndrome requires a multi-modal approach. The goals of treatment are normalization of cortisol excess, long-term disease control, avoidance of recurrence, and reversal of clinical features.[4]

Guidelines

The Endocrine Society published clinical practice guidelines for the treatment of Cushing's syndrome in (2015) and Cushing's disease (2021).[5,6] 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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Signifor LAR. 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

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.

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 BOTH 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.

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.

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; August 2023.
2. Sharma ST, Nieman LK, Feelders RA. Cushing's syndrome: epidemiology and developments in disease management. *Clin Epidemiol*. 2015;7:281–293.
3. Tritos NA, Biller BM. Advances in medical therapies for Cushing's syndrome. *Discov Med*. 2012;13(69):171-179.
4. Biller BMK, Grossman AB, Stewart PM, et al. Treatment of adrenocorticotropin-dependent Cushing's syndrome: A consensus statement. *J Clin Endocrinol Metab*. 2008;93:2454-2462.
5. 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.
6. 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.