PRIOR AUTHORIZATION POLICY

POLICY: Cushing's – Signifor Prior Authorization Policy
- Signifor™ (pasireotide subcutaneous injection – Novartis)

REVIEW DATE: 04/19/2024

OVERVIEW

Signifor, a somatostatin analog, is indicated for the treatment of **Cushing's disease** in adults for whom pituitary surgery is not an option or has not been curative.[1]

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 (2015) for the treatment of Cushing's syndrome.[5] First-line treatment involves resection of the tumor, unless surgery is not possible or is unlikely to meaningfully reduce excess glucocorticoid levels. In patients with ACTH-dependent Cushing's syndrome who underwent non-curative 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 medical therapies as second-line options after transsphenoidal surgery: steroidogenesis inhibitors (ketoconazole tablets, Metopirone® [metyrapone capsules], Lysodren® [mitotane tablets], etomidate injection) in patients either with or without radiotherapy/radiosurgery; pituitary-directed medical treatments (cabergoline tablets, Signifor) in patients who are not surgical candidates or who have persistent disease; and mifepristone tablets (Korlym®, generic) 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. 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 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

1. **Cushing's Disease.** Approve for the duration noted below if the patient meets ONE of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 4 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** According to the prescriber, the patient is not a candidate for surgery or surgery has not been curative; AND
       Note: For patients with endogenous Cushing's syndrome awaiting surgery or therapeutic response after radiotherapy, see *Other Uses with Supportive Evidence*.
     - **iii.** The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of Cushing's syndrome.
   - **B)** Patient is Currently Receiving Signifor/Signifor LAR. Approve for 1 year if the patient has had a response, as determined by the prescriber; and patient is continuing therapy to maintain response.

Other Uses with Supportive Evidence

2. **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 specializes in the treatment of Cushing's syndrome.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Signifor 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® subcutaneous injection [prescribing information]. Lebanon, NJ: Recordati Rare Diseases; March 2020.
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.