Reference number(s)
2749-A

Standard Medicare Part B Management Signifor LAR

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Signifor LAR	pasireotide

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications[1]

- Treatment of patients with acromegaly who have had an inadequate response to surgery and/or for whom surgery is not an option.
- Treatment of patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

Compendial Uses[2]

- Carcinoid syndrome.
- Metastatic neuroendocrine tumors (NETs) of the gastrointestinal (GI) tract (carcinoid tumors).

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Documentation

The following documentation must be available, upon request, for all submissions:

Acromegaly:

- For initial approval: Laboratory report indicating high pretreatment insulin-like growth factor-1 (IGF-1) level and chart notes indicating an inadequate or partial response to surgery or a clinical reason for not having surgery.
- For continuation: Laboratory report indicating normal current IGF-1 levels or chart notes indicating that the member's IGF-1 level has decreased or normalized since initiation of therapy.

Cushing's Disease:

- For initial requests, pretreatment cortisol level as measured by one of the following tests:
  - Urinary free cortisol (UFC)
  - Late-night salivary cortisol
  - 1 mg overnight dexamethasone suppression test (DST)
  - Longer, low dose DST (2 mg per day for 48 hours)
- For continuation of therapy (if applicable), laboratory report indicating current cortisol level has decreased from baseline as measured by one of the following tests:
  - Urinary free cortisol (UFC)
  - Late-night salivary cortisol
  - 1 mg overnight dexamethasone suppression test (DST)
  - Longer, low dose DST (2 mg per day for 48 hours)

Coverage Criteria

Acromegaly[1,3,4]

Authorization of 12 months may be granted for treatment of acromegaly when all of the following criteria are met:

- Member has a high pretreatment insulin-like growth factor-1 (IGF-1) level for age and/or gender based on the laboratory reference range.
- Member has had an inadequate or partial response to surgery OR there is a clinical reason why the member has not had surgery.

Cushing's Disease[1,5]

Authorization of 12 months may be granted for treatment of Cushing's disease when the member has had surgery that was not curative OR the member is not a candidate for surgery.

Neuroendocrine Tumors (NETs) of the Gastrointestinal (GI) Tract (Carcinoid Tumors)[2]

Authorization of 12 months may be granted for treatment of metastatic NETs of the GI tract (carcinoid tumors).

Carcinoid Syndrome[2]

Authorization of 12 months may be granted for treatment of carcinoid syndrome.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat an indication in the coverage criteria section.
- The member is receiving benefit from therapy. Benefit is defined as:
    - Acromegaly: decreased or normalized IGF-1 level since initiation of therapy.
    - Cushing's disease (any of the following):
        - Lower cortisol levels since the start of therapy per one of the following tests:
            - Urinary free cortisol (UFC)
            - Late-night salivary cortisol
            - 1 mg overnight dexamethasone suppression test (DST)
            - Longer, low dose DST (2 mg per day for 48 hours)
        - Improvement in signs and symptoms of the disease
    - All other indications: improvement or stabilization of clinical signs and symptoms since initiation of therapy.

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Signifor LAR.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- Acromegaly: an endocrine society clinical practice guideline.
- American Association of Clinical Endocrinologists Acromegaly Guidelines Task Force. Medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update.
- Treatment of Cushing's syndrome: An Endocrine Society Clinical Practice Guideline.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Signifor LAR are covered in addition to the following:

- Carcinoid syndrome

- Metastatic neuroendocrine tumors (NETs) of the gastrointestinal (GI) tract (carcinoid tumors)

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Signifor LAR to treat carcinoid syndrome and metastatic neuroendocrine tumors (NETs) of the gastrointestinal tract can be found in the Micromedex DrugDex database. Use of information in the DrugDex database for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Support for utilizing a high pretreatment insulin-like growth factor-1 (IGF-1) as a diagnostic requirement and targeting IGF-1 in patients with acromegaly is supported by two professional guidelines.

According to Katznelson et al, the biochemical target goal is an age-normalized IGF-1. An age-normalized IGF-1 signifies control of acromegaly.

According to the Endocrine Society, IGF-1 should be measured and patients with elevated or equivocal serum IGF-1 levels should have the diagnosis confirmed by finding lack of suppression of growth hormone to less than 1 microgram/L following documented hyperglycemia during an oral glucose load. The Endocrine Society also supports the normalization of IGF-1 as the biochemical target goal of therapy with Signifor LAR.

References

1. Signifor LAR [package insert]. Bridgewater, NJ: Recordati Rare Diseases Inc; July 2024.
2. IBM Micromedex® DRUGDEX® (electronic version). Micromedex Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com [available with subscription]. Accessed November 8, 2024.
3. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014;99:3933-3951.
4. American Association of Clinical Endocrinologists Acromegaly Guidelines Task Force. Medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update. Endocr Pract. 2011;17(suppl 4):1-44.
5. Nieman LK, Biller BM, Findling JW, et al. Treatment of Cushing's syndrome: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015;100(8):2807-31.
6. Gadelha MR, Bronstein MD, Brue T, et al. Pasireotide versus continued treatment with octreotide or lanreotide in patients with inadequately controlled acromegaly (PAOLA): a randomized, phase 3 trial. Lancet Diabetes Endocrinol. 2014;2:875-84.
7. Colao A, Bronstein MD, Freda P, et al. Pasireotide versus octreotide in acromegaly: a head-to-head superiority study. J Clin Endocrinol Metab. 2014;99:791–799.