Clinical Policy: Pasireotide (Signifor LAR)

Reference Number: CP.PHAR.332
Effective Date: 03/17
Last Review Date: 02/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The intent of these criteria is to ensure that patients follow selection elements established by Centene® clinical policy for pasireotide for intramuscular injection (Signifor® LAR [Long-Acting Release])*.

**Signifor LAR for intramuscular injection should not be confused with Signifor for subcutaneous injection FDA labeled for Cushing's disease.*

Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation® that Signifor LAR is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acromegaly (must meet all):

1. Prescribed by or in consultation with an endocrinologist;
2. Diagnosis of acromegaly (see Appendix B for an overview of acromegaly);
3. Age ≥ 18 years or, if younger, epiphyseal growth plates have closed*;
4. Failure to achieve full biochemical control† after ≥ 3 months on either of the following somatostatin analogs at a maximally tolerated dose (unless intolerant or contraindicated):
   a. Long-acting octreotide (Sandostatin LAR);
   b. Lanreotide (Somatuline Depot);
5. Member does not have severe hepatic impairment (Child-Pugh C);
6. Prescribed dose does not exceed:
   a. 40 mg every 4 weeks if a new start;
   b. 60 mg every 4 weeks if not a new start.

**Growth Hormone (GH) excess occurring in growing children/adolescents before epiphyseal growth plate closure (known as pituitary gigantism) is not included in the present policy given unique etiologic and management considerations and relative lack of evidence of Signafor LAR versus other somatostatin analogs in this setting.*[2,6,8]

†Full biochemical control when receiving somatostatin analog therapy (including Signifor LAR) is defined as a random GH serum concentration of < 1 nanogram (ng)/mL AND a normal age- and sex-adjusted insulin growth factor-1 [IGF-1] serum concentration. (Demonstration of GH suppression via an oral glucose tolerance test is not optimal when receiving somatostatin analog therapy given complicating interactions across somatostatin analogs, growth hormone and insulin.)[2,3,6]

Approval duration: 3 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 – Global Biopharm Policy.

II. Continued Approval

A. Acromegaly (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. If has taken Signifor LAR for ≥ 12 months, improvement in biochemical control (i.e., any decrease in random GH or age- and sex-adjusted IGF-1 serum concentrations since baseline*) or in tumor mass control;
3. Prescribed current or new dose does not exceed 60 mg every 4 weeks;
4. If request is for a dose increase, meets all of the following:
   a. Member has been on the current dose for ≥ 3 months;
   b. The current dose has not resulted in full biochemical control†;
   c. Requested dose increase does not exceed an additional 20 mg every 4 weeks;
5. Member has none of the following reasons to discontinue:
   a. Severe hepatic impairment (Child-Pugh C).

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**Any improvement short of full biochemical control may result in beneficial clinical outcomes; combination therapy may be necessary to achieve additional biochemical control.*[2,3,6]

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:
Signifor LAR is an injectable cyclohexapeptide somatostatin analog (often referred interchangeably as a somatostatin analog or somatostatin receptor ligand [SRL]). Pasireotide exerts its pharmacological activity (suppression of GH secretion) via binding to somatostatin receptors (SSTR). There are five human somatostatin receptor subtypes: SSTR 1, 2, 3, 4, and 5. These receptor subtypes are expressed in different tissues under normal physiological conditions. Somatostatin analogs bind to SSTRs with different potencies. Pasireotide binds with high affinity to four of the five SSTRs.

Formulations:
Signifor LAR (pasireotide) for injectable suspension is supplied in a single-use kit containing 20 mg, 40 mg, or 60 mg of Signifor LAR powder for reconstitution:

- After reconstitution of the 20 mg, 40 mg, or 60 mg Signifor LAR vials with the provided 2 mL diluent, the injectable suspension will have a final concentration of 10 mg/mL, 20 mg/mL and 30 mg/mL respectively.

FDA Approved Indications:
Signifor LAR is a somatostatin analog/intramuscular formulation indicated for:

- Treatment of patients with acromegaly who have had an inadequate response to surgery and/or for whom surgery is not an option.

Appendices

Appendix A: Abbreviation Key

GH: Growth hormone
GHRH: Growth hormone-releasing hormone
IGF-1: Insulin growth factor 1
LAR: Long-acting release
SRL: Somatostatin receptor ligand
SSTR: Somatostatin receptor

Appendix B: Acromegaly Overview[2-7]

- Definition
  - Acromegaly is a chronic disorder caused by overproduction of growth hormone (GH) usually from the pituitary gland. Insulin-like growth factor 1 (IGF-1) from the liver and other tissues is stimulated by excess GH giving rise to associated clinical manifestations (enlargement of facial features, hands and feet) and comorbidities.
- Diagnosis
  - Diagnosis is suspected based on a constellation of some or all of the following:
    - Clinical features, comorbidities, pituitary mass.
  - Diagnosis is supported with biochemical testing and imaging:
    - Biochemical findings suggesting acromegaly include equivocal to high IGF-1 and, if needed, inadequate suppression of GH to < 1 ng/mL following an oral glucose load.
    - Imaging investigates the presence/absence of an associated pituitary adenoma *(present approximately 95% of the time)* or other tumor.
- Causes of acromegaly
  - GH excess
    - Primary GH excess (pituitary origin)
    - Ectopic or iatrogenic GH excess
    - GH excess due to familial syndromes
  - Growth hormone releasing hormone (GHRH) excess
    - Central ectopic (<1 percent); hypothalamic hamartoma, choristoma, ganglioneuroma
- Clinical features and associated comorbidities
  - Clinical features: Enlargement of facial and acral (hands/feet) features
  - Associated comorbidities:
    - Examples: Sleep apnea syndrome, type 2 diabetes mellitus, debilitating arthritis, carpal tunnel syndrome, hyperhidrosis, hypertension, cardiovascular disease.
    - If presence of a pituitary or hypothalamic tumor, problems related to tumor size such as headache or visual loss.
- Treatment goals
  - Inhibition of GH hypersecretion and normalization of IGF-I levels
  - Improvement in comorbidities and clinical features if present (GH excess may be relatively asymptomatic)
  - Reduction or control of tumor growth if applicable
  - Maintenance of pituitary function
- Treatment modalities*
  - Surgery - if disease is associated with a tumor and surgery is appropriate
  - Medical management
    - Somatostatin analogs

- Long-acting octreotide (Sandostatin LAR)
- Lanreotide (Somatuline Depot)
- Pasireotide (Signifor LAR)

▪ Dopamine agonists (cabergoline)
▪ GH receptor antagonist (pegvisomant)

o Radiotherapy

**Combination therapy may be necessary.*

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2502	Pasireotide (Signifor LAR)

Reviews, Revisions, and Approvals	Date	Approval Date
Policy split from CP.PHAR.183.Excellus Other Specialty Pharmacy. Initial therapy:"In consultation with" is added to "prescribed by an endocrinologist." "Epiphyseal growth plates have closed" is added to "age ≥ 18 years." Definition of full biochemical control is updated per the 2014 Endocrine Society guidelines and includes a tightening of random GH levels from < 2.5 ng/mL to < 1.0 ng/mL.[2] Hepatic impairment restriction is added per PI. Dosing follows PI recommendations. Continued therapy: Demonstrated response does not include surgery outcomes, is not required until after 12 months of therapy, and is limited to any degree of improvement in biochemical control. Response criteria related to clinical features or comorbidities are not included as GH excess may be relatively asymptomatic.	02/17	03/17 (Specialist reviewed 02/17)

References
1. Signifor LAR prescribing information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2014. Available at https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/signifor_lar.pdf. Accessed February 7, 2017.
2. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2014; 99(11): 3933-3951.
3. Melmed S, Colao A, Barkan A, et al. Guidelines for acromegaly management: An update. J Clin Endocrinol Metab. 2009; 94:1509–1517.

4. Melmed S. Causes and clinical manifestations of acromegaly. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at www.UpToDate.com. Accessed February 8, 2017.
5. Melmed S. Diagnosis of acromegaly. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at www.UpToDate.com. Accessed February 8, 2017.
6. Melmed S. Treatment of acromegaly. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at www.UpToDate.com. Accessed February 8, 2017.
7. Colao A, Ferone D, Marzullo P, et al. Systemic complications of acromegaly: Epidemiology, pathogenesis, and management. Endocr Rev. 2004; 25(1): 102.
8. Eugster EA. Pituitary gigantism. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at www.UpToDate.com. Accessed February 8, 2017.

Important reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.