Clinical Policy: Pasireotide (Signifor LAR)

Reference Number: CP.PHAR.332
Effective Date: 03.01.17
Last Review Date: 11.17
Line of Business: Medicaid

Coding Implications
Revision Log

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

Description
Pasireotide (Signifor LAR®) is somatostatin analog.

FDA Approved Indication(s)
Signifor LAR is indicated for the treatment of patients with acromegaly who have had an inadequate response to surgery and/or for whom surgery is not an option.

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

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval 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. Diagnosis of acromegaly (see Appendix B for an overview of acromegaly);
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 18 years;
4. Failure to achieve full biochemical control (see Appendix C) after ≥ 3 months on either of the following somatostatin analogs at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced:
   a. Long-acting octreotide (Sandostatin LAR);
   b. Lanreotide (Somatuline Depot);
5. 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.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Acromegaly (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy [if taken Signifor LAR for ≥ 12 months, improvement in biochemical control (i.e., any decrease in random growth hormone [GH] or age- and sex-adjusted insulin growth factor 1 [IGF-1] serum concentrations since baseline or in tumor mass control)];
3. If request is for a dose increase, new dose meets all of the following (a-d):
   a. Member has been on the current dose for ≥ 3 months;
   b. The current dose has not resulted in full biochemical control (see Appendix C);
   c. Requested dose increase does not exceed an additional 20 mg every 4 weeks;
   d. Current or new dose does not exceed 60 mg every 4 weeks.

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.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

GH: growth hormone
GHRH: growth hormone-releasing hormone
IGF-1: insulin growth factor 1
LAR: long-acting release

Appendix B: Acromegaly Overview

- Definition
  - Acromegaly is a chronic disorder caused by overproduction of GH usually from the pituitary gland. 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)
    - Radiotherapy

**Combination therapy may be necessary.*

Appendix C: General Information
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]

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Acromegaly	40 mg IM once every 4 weeks	60 mg IM every 4 weeks

VI. Product Availability

Injectable suspension: 20 mg, 40 mg, and 60 mg

VII. 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 August 20, 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.

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	P&T 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.	02.01.17	03.17 (Specialist reviewed 02/17)
Updated references and new template. Changed initial approval duration from 3 to 6 months	08.20.17	11.17

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.

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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.