Clinical Policy: Pasireotide (Signifor, Signifor LAR)

Reference Number: CP.PHAR.332
Effective Date: 03.01.17
Last Review Date: 11.22
Line of Business: Commercial, HIM*, Medicaid

Coding Implications
Revision Log

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

Description

Pasireotide (Signifor®, Signifor® LAR) is a somatostatin analog.

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***For Health Insurance Marketplace (HIM),** if request is through pharmacy benefit, Signifor LAR is non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

FDA Approved Indication(s)

Signifor and Signifor LAR are indicated for the treatment of patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative. Signifor is specifically indicated in adults.

Signifor LAR is also 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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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

I. Initial Approval Criteria

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

1. Diagnosis of acromegaly as evidenced by one of the following (a or b):
   a. Pre-treatment insulin-like growth factor-I (IGF-I) level above the upper limit of normal based on age and gender for the reporting laboratory;
   b. Serum growth hormone (GH) level ≥ 1 µg/mL after a 2-hour oral glucose tolerance test;
2. Request is for Signifor LAR;
3. Prescribed by or in consultation with an endocrinologist;
4. Age ≥ 18 years;
5. Inadequate response to surgical resection or pituitary irradiation (*see Appendix D*), or member is not a candidate for such treatment;
6. Dose does not exceed (a and b):
   a. 60 mg every 4 weeks;
   b. 1 vial every 4 weeks.

Approval duration:
Medicaid – 6 months

HIM – *refer to HIM.PA.103 for Signifor LAR*
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Cushing's Disease (must meet all)**:**
1. Diagnosis of Cushing's disease;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Pituitary surgery was not curative;
   b. Member is not eligible for pituitary surgery;
5. Dose does not exceed one of the following (a or b):
   a. Signifor (i and ii):
      i. 1.8 mg per day;
      ii. 2 ampules per day;
   b. Signifor LAR (i and ii):
      i. 40 mg every 4 weeks
      ii. 1 vial every 4 weeks.

Approval duration:
Medicaid – 6 months
HIM – 6 months for Signifor (*refer to HIM.PA.103 for Signifor LAR*)
Commercial – 6 months or to the member's renewal date, whichever is longer

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Acromegaly (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);

2. Request is for Signifor LAR;
3. Member is responding positively to therapy (*see Appendix D*);
4. If request is for a dose increase, new dose does not exceed (a and b):
   a. 60 mg every 4 weeks;
   b. 1 vial every 4 weeks.

Approval duration:
Medicaid – 12 months
HIM – *refer to HIM.PA.103 for Signifor LAR*
Commercial – 12 months or to the member's renewal date, whichever is longer

B. Cushing's Disease (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy (*see Appendix D*);
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Signifor (i and ii):
      i. 1.8 mg per day;
      ii. 2 ampules per day;
   b. Signifor LAR (i and ii):
      i. 40 mg every 4 weeks;
      ii. 1 vial every 4 weeks.

Approval duration:
Medicaid – 12 months
HIM – 12 months for Signifor (*refer to HIM.PA.103 for Signifor LAR*)
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
GH: growth hormone
IGF-I: insulin-like growth factor

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information

- Treatment response for Cushing's disease may be defined as reduction in 24-hour urinary free cortisol (UFC) levels and/or improvement in signs or symptoms of the disease. Maximum urinary free cortisol reduction is typically seen by two months of treatment.
- Examples of treatment response to acromegaly therapy (including somatostatin analogs, surgical resection or pituitary irradiation) include improvement from baseline in or normalization of GH and/or age- and sex-adjusted IGF-I serum concentrations, or tumor mass control.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Pasireotide (Signifor)	Cushing's disease	Initial: 0.6 mg or 0.9 mg SC BID Recommended dosing range: 0.3 mg to 0.9 mg SC BID	1.8 mg/day
Pasireotide (Signifor LAR)*	Cushing's disease	10 mg to 40 mg IM every 4 weeks	40 mg/4 weeks
	Acromegaly	40 mg to 60 mg IM every 4 weeks	60 mg/4 weeks

**Signifor LAR must be administered by a healthcare professional*

VI. Product Availability

Drug Name	Availability
Pasireotide (Signifor)	Single-dose ampules for injection: 0.3 mg/mL, 0.6 mg/mL, 0.9 mg/mL
Pasireotide (Signifor LAR)	Vials for reconstitution and injectable suspension: 10 mg, 20 mg, 30 mg, 40 mg, 60 mg

VII. References

1. Signifor Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2020. Available at: https://www.signifor.com/pdf/signifor-pi.pdf. Accessed July 20, 2022.
2. Signifor LAR Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2020. Available at https://www.signiforlar.com/pdf/signifor-lar-pi.pdf. Accessed July 20, 2022.
3. Melmed S, Bronstein MD, Chanson P. A Consensus Statement on acromegaly therapeutic outcomes. Nat Rev Endocrinol. 2018 Sep;14(9):552-561.
4. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2014; 99(11): 3933-3951.
5. Fleseriu M, Biller BMK, Freda PU, et al. A Pituitary Society update to acromegaly management guidelines. Pituitary. 2021; 24: 1-13.
6. Guistina A, Barkhoudarian G, Beckers A, et al. Multidisciplinary management of acromegaly: A consensus. Rev Endocr Metab Disord. 2020; 21(4): 667-678.
7. Nieman LK, Biller BMK, Findling JW, et al. Treatment of Cushing's syndrome: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2015; 100(8): 2807-2831.
8. 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.

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	Injection, pasireotide long acting, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2018 annual review: policy combined with commercial policy CP.CPA.152 and HIM policy HIM.PA.SP54; Signifor added to policy; criteria added for new FDA indication for Signifor LAR: Cushing's disease; new strengths of Signifor LAR added; specialist requirement was added for commercial; age requirement was added for commercial; trial of octreotide or lanreotide for acromegaly	08.14.18	11.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
removed for Medicaid; requirement for inadequate response to surgery or pituitary irradiation added for acromegaly; initial approval duration for acromegaly for Medicaid revised to 3 months to allow for dose adjustment; specific requirements for positive response to therapy for acromegaly moved to appendix for Medicaid; simplified max dose requirement for Signifor LAR for Medicaid; references reviewed and updated.		
4Q 2019 annual review: increased acromegaly initial approval duration from 3 months to 6 months to align with approach for other acromegaly policies; added HIM-Medical Benefit line of business; references reviewed and updated.	08.27.19	11.19
4Q 2020 annual review: removed HIM-Medical Benefit line of business; references reviewed and updated.	08.11.20	11.20
4Q 2021 annual review: no significant changes; updated J code; modified reference from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated	08.12.21	11.21
4Q 2022 annual review: for acromegaly, added confirmatory diagnostic requirements (IGF-I or GH) per PS/ES practice guidelines; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	07.20.22	11.22

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.