Clinical Policy: Pasireotide (Signifor, Signifor LAR)

Reference Number: PA.CP.PHAR.332
Effective Date: 01/2018
Last Review Date: 01/2026

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

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
It is the policy of PA Health and Wellness® that Signifor and Signifor LAR is **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. Failure of both of the following^, unless clinically significant adverse effects are experienced or all are contraindicated (a and b);
   a. Lanreotide (Somatuline® Depot);
   b. Both of the following (i and ii):
      i. Generic octreotide acetate LAR (generic Sandostatin® LAR Depot), unless octreotide acetate LAR is unavailable due to shortage;
      ii. If member is unable to use generic octreotide acetate LAR (generic Sandostatin LAR Depot) due to shortage: Sandostatin LAR Depot;

   ^Prior authorization may be required for lanreotide, octreotide acetate LAR, and Sandostatin LAR Depot
7. Dose does not exceed (a and b):
   a. 60 mg every 4 weeks;
   b. 1 vial every 4 weeks.

Approval duration: 12 months

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. Ineligible 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: 12 months

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Acromegaly (must meet all):
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.PHARM.01) applies;
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: 12 months

B. Cushing's Disease (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.PHARM.01) applies;
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: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53
   a. The requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use.

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 – PA.CP.PMN.53 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
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
octreotide acetate (Sandostatin LAR Depot) [IM]	20-40 mg IM every 4 weeks	See dosing regimen
lanreotide (Somatuline Depot)	90-20 mg SC every 4 weeks	See dosing regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

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 growth hormone (GH) and/or age- and sex-adjusted insulin-like growth factor (IGF-1) 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*

IV. 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)	Vial for reconstitution and injectable suspension: 10 mg, 20 mg, 30 mg, 40 mg, 60 mg

VI. References

1. Signifor Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2024. Available at: https://www.signifor.com/pdf/signifor-pi.pdf. Accessed July 10, 2025.
2. Signifor LAR Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2024. Available at https://www.signiforlar.com/pdf/signifor-lar-pi.pdf. Accessed July 10, 2025.
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. Giustina A, Biermasz N, Casanueva FF, et al; Acromegaly Consensus Group (ACG). Consensus on criteria for acromegaly diagnosis and remission. Pituitary. 2024 Feb;27(1):7-22. doi: 10.1007/s11102-023-01360-1.
7. Guistina A, Barkhoudarian G, Beckers A, et al. Multidisciplinary management of acromegaly: A consensus. Rev Endocr Metab Disord. 2020; 21(4): 667-678.
8. 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.
9. 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
J3490	Unclassified drugs

Reviews, Revisions, and Approvals	Date
4Q 2018 annual review: Signifor added to policy; criteria added for new FDA indication for Signifor LAR: Cushing's disease; new strengths of Signifor LAR added; requirement for inadequate response to surgery or pituitary irradiation added for acromegaly; references reviewed and updated.	08/2018
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: increased acromegaly initial approval duration from 3 months to 6 months to align with approach for other acromegaly policies; references reviewed and updated.	08/2020
4Q 2021 annual review: no significant changes; updated J code; references reviewed and updated	10/2021
4Q 2022 annual review: for acromegaly, added confirmatory diagnostic requirements (IGF-I or GH) per PS/ES practice guidelines; references reviewed and updated.	10/2022
4Q 2023 annual review: no significant changes; added J3490 code for Signifor; references reviewed and updated.	10/2023
4Q 2024 annual review: for acromegaly, revised initial criteria from "(GH) level ≥ 1 µg/mL" to "(GH) level ≥ 1 µg/L" per PS/ES practice guidelines and ACG; references reviewed and updated.	10/2024
4Q 2025 annual review: no significant changes; for acromegaly, extended initial approval duration from 6 months to 12 months; for cushing's disease, extended initial approval duration from 6 months to 12 months; references reviewed and updated.	10/2025
Per December SDC, added redirection to all of the following: lanreotide, octreotide acetate LAR (generic Sandostatin LAR Depot), and brand Sandostatin LAR Depot if octreotide acetate LAR (generic Sandostatin LAR Depot) is unavailable due to shortage.	01/2026