Clinical Policy: Pasireotide (Signifor, Signifor LAR)

Reference Number: PA.CP.PHAR.332
Effective Date: 01.18
Last Review Date: 10/18

Coding Implications
Revision Log

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

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

FDA Approved Indication(s)
Signifor is indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

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
- Patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania 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;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 18 years;
4. Request is for Signifor LAR;
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 60 mg every 4 weeks (1 vial every 4 weeks).

Approval duration: 36 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: 1.8 mg per day (2 ampules per day);
b. Signifor LAR: 40 mg every 4 weeks (1 vial every 4 weeks).

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

II. Continued Approval

A. Acromegaly (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (*see Appendix D*);
3. Request is for Signifor LAR;
4. If request is for a dose increase, new dose does not exceed 60 mg every 4 weeks (1 vial every 4 weeks).

Approval duration: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.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. Signifor: 1.8 mg per day (2 ampules per day);
   b. Signifor LAR: 40 mg every 4 weeks (1 vial every 4 weeks).

Approval duration: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to CP.PMN.53

III. 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
Pasireotide (Signifor LAR)*	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 injection: 10 mg, 20 mg, 30 mg, 40 mg, 60 mg

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.

Appendices

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

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 growth hormone (GH) and/or age- and sex-adjusted insulin-like growth factor (IGF-1) serum concentrations, or tumor mass control.

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
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.	08/18	

References
1. Signifor Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2018. Available at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/signifor.pdf?site=PC. Accessed August 14, 2018.
2. Signifor LAR Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2018. Available at https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/signifor_lar.pdf. Accessed August 14, 2018.
3. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2014; 99(11): 3933-3951.
4. Melmed S, Colao A, Barkan A, et al. Guidelines for acromegaly management: An update. J Clin Endocrinol Metab. 2009; 94:1509–1517.
5. Katznelson L, Atkinson JLD, Cook DM, Ezzat SZ, Hamrahian AH, Miller KK. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update. Endocrine Practice. 2011;17(Suppl 4).