Clinical Policy: Pasireotide (Signifor, Signifor LAR)

Reference Number: ERX.SPA.212
Effective Date: 01.11.17
Last Review Date: 11.22
Line of Business: Commercial, Medicaid

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.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Signifor and Signifor LAR **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: 6 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. 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: 6 months

C. Other diagnoses/indications
1. Refer to ERX.PA.01 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 a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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 a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 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 – ERX.PA.01 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 clinically meaningful 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	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 August 12, 2021.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2018 annual review: criteria added for new FDA indication for Signifor LAR: Cushing's disease; new strengths of Signifor LAR added; simplified max dose requirement of Signifor LAR for acromegaly; initial approval duration for acromegaly revised to 3 months to allow for dose adjustment; requirement for inadequate response to surgery or pituitary irradiation added for acromegaly; specific requirements for positive response to therapy for acromegaly moved to appendix; references reviewed and updated.	08.14.18	11.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2019 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.	08.27.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.11.20	11.20
4Q 2021 annual review: no significant changes; references reviewed and updated.	08.25.21	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.	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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.