Signifor® LAR (pasireotide)
(Intramuscular)

Effective Date: 01/01/2020
Review Date: 12/20/2019, 9/14/2020, 06/24/2021, 9/02/2021, 01/20/2022, 02/23/2023, 12/07/2023, 01/10/2024, 05/28/2025, 02/10/2026

Scope: Medicaid, Commercial, Medicare

Length of Authorization

Coverage is provided for six months and may be renewed.

I. Dosing Limits

A. Max Units (per dose and over time) [HCPCS Unit]:

Acromegaly

- 60 billable units (60mg) every 28 days

Cushing's disease

- 40 billable units (40mg) every 28 days

II. Summary of Evidence

Signifor LAR (pasireotide pamoate) is a long-acting somatostatin analog 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. It is also indicated for the treatment of Cushing's disease in patients who require pharmacologic intervention and for whom surgery has failed or is not an option. Approval in acromegaly is supported by a randomized, double-blind, active-controlled Phase III trial in 198 patients previously treated with somatostatin analogs. Patients were randomized to receive Signifor LAR 40 mg or 60 mg intramuscularly every 4 weeks. At month 12, 15% of patients in the 40 mg group and 20% in the 60 mg group achieved biochemical control (GH <2.5 ng/mL and normalized IGF-1) compared to 0% in the octreotide LAR group ($p<0.05$). Approval in Cushing's disease is based on a multicenter, randomized, Phase III trial in 150 patients with persistent or recurrent disease. Patients received 10 mg or 30 mg every 4 weeks for 12 months. At Month 7, 41% of patients in the 10 mg group and 30% in the 30 mg group achieved normalized 24-hour urinary free cortisol (UFC), with maintained biochemical response through month 12 in most responders. The most common adverse reactions (≥10%) include diabetes mellitus, hyperglycemia, diarrhea, cholelithiasis, abdominal pain, nausea, and fatigue. Serious hyperglycemia-related adverse events were reported, and new-onset or worsening diabetes is a significant risk requiring regular monitoring and management. QT prolongation, bradycardia, and liver enzyme elevations have also been observed.

III. Initial Approval Criteria[1,4,5,6,9]

Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Universal Criteria

- Member is at least 18 years old; **AND**
- Prescribed by or in consultation with an endocrinologist; **AND**
- Member does not have severe hepatic impairment (i.e., Child-Pugh Class C); **AND**
- Member has not received a long-acting somatostatin analogue (e.g., octreotide LAR, lanreotide SR, lanreotide autogel, pasireotide LAR, etc.) within the last 4 weeks; **AND**

Acromegaly †

- Diagnosis of acromegaly has been confirmed by one of the following:
  - Serum GH level > 1ng/ml after 2-hour OGTT at time of diagnosis; OR
  - Elevated serum insulin-like growth factor-1 (IGF-1) [above the age and gender adjusted normal range per physician's lab] at diagnosis; **AND**
- Member has documented inadequate response to surgery and/or radiotherapy or it is not an option for the member; **AND**
- Baseline growth hormone (GH) and IGF-1 blood levels have been obtained (renewal will require reporting of current levels); **AND**
- Will not be used in combination with oral octreotide or with GH-analogues (e.g., pegvisomant); **AND**
- Member must have a documented failure, intolerance or contraindication to Somatuline Depot (lanreotide) or Sandostatin LAR Depot (octreotide acetate)

Cushing's Disease † Φ

- Confirmed diagnosis of endogenous Cushing's disease in which the member's hypercortisolism is not a result of chronic administration of high-dose glucocorticoids or other physiologic conditions; **AND**
- Treatment of member's disease with pituitary surgery has not been curative OR the member is not a candidate for pituitary surgery; **AND**
- Baseline 24-hour urinary free cortisol (UFC) level, adrenocorticotropic hormone (ACTH), and/or serum cortisol level have been obtained (renewal will require reporting of current levels)

† FDA Approved Indication(s); Φ Orphan Drug

IV. Renewal Criteria[1,4,5,6,9]

Coverage can be renewed based upon the following criteria:

- Member continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include : uncontrolled hyperglycemia, diabetes, ketoacidosis, bradycardia, QT prolongation, liver test elevations (e.g., alanine aminotransferase [ALT] or aspartate aminotransferase [AST]), cholelithiasis (gallstones) and complications of cholelithiasis (e.g., cholecystitis or cholangitis), pituitary hormone (e.g., thyroid, adrenal, gonadal)

deficiencies/severe adrenal insufficiency, etc gallstones (cholelithiasis), pituitary hormone deficiency, etc.; **AND**

Acromegaly

- Disease response as indicated by an improvement in signs and symptoms compared to baseline; **AND**
    - Reduction of growth hormone (GH) from pretreatment baseline; **OR**
    - Age-adjusted normalization of serum IGF-1

Cushing's Disease

- Disease response indicated by reduction in urinary free cortisol (UFC), plasma adrenocorticotropic hormone (ACTH), and/or serum cortisol levels from baseline

V. Dosage/Administration[1]

Indication	Dose
Acromegaly	Initiate at 40 mg by intramuscular injection once every 4 weeks (28 days). – Titrate dosage based on treatment response and tolerability up to maximum 60 mg every 4 weeks for members who have not normalized GH and/or IGF-1 levels after 3 months of treatment with the 40 mg dose.
Cushing's Disease	Initiate at 10 mg by intramuscular injection once every 4 weeks (28 days). – Titrate dosage based on treatment response and tolerability up to maximum 40 mg every 4 weeks for members who have not normalized 24-hour urinary free cortisol (UFC) after 4 months of treatment with the 10mg dose.

VI. Billing Code/Availability Information

HCPCS code:

- J2502 - Injection, pasireotide long acting, 1 mg; 1 billable unit = 1 mg

NDC:

- Signifor LAR 10 mg kit: 00078-0748-xx
- Signifor LAR 20 mg kit: 00078-0641-xx
- Signifor LAR 30 mg kit: 00078-0741-xx
- Signifor LAR 40 mg kit: 00078-0642-xx
- Signifor LAR 60 mg kit: 00078-0643-xx

VII. References

1. Signifor [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation; July 2024. Accessed December 2025.

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8. Hur KY, Kim JH, Kim BJ, et al. Clinical Guidelines for the Diagnosis and Treatment of Cushing's Disease in Korea. Endocrinol Metab (Seoul). 2015 Mar; 30(1): 7–18.
9. Nieman LK, Biller BMK, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 8, 1 August 2015, Pages 2807–2831.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E22.0	Acromegaly and pituitary gigantism
E34.4	Constitutional tall stature
E24.0	Pituitary-dependent Cushing's disease

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Signifor was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Signifor according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.