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

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

Length of Authorization

Coverage is provided for six months and may be renewed.

I. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Signifor LAR 10 mg kit: 1 kit per 28 days
- Signifor LAR 20 mg kit: 1 kit per 28 days
- Signifor LAR 30 mg kit: 1 kit per 28 days
- Signifor LAR 40 mg kit: 1 kit per 28 days
- Signifor LAR 60 mg kit: 1 kit per 28 days

B. 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 is a somatostatin analog indicated for treatment of acromegaly and Cushing's disease. Clinical trials outcomes included reduction in GH and IGF-1 levels, symptom improvement, and tumor shrinkage in certain patients. Common adverse reactions are gastrointestinal symptoms (e.g., diarrhea, nausea, abdominal pain), hyperglycemia, and injection site reactions.

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

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

Coverage is provided in the following conditions:

- Patient is at least 18 years old; **AND**

- Confirmation that fasting plasma glucose, hemoglobin A1c, liver enzyme tests, electrocardiogram (ECG), serum magnesium and serum potassium have been evaluated prior to starting treatment; **AND**
- Patients with diabetes mellitus have stable glycemic control and are on optimized anti-diabetic treatment prior to the start of therapy; **AND**

Universal Criteria

- Patient does not have severe hepatic impairment (i.e., Child-Pugh Class C); **AND**
- Patient 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 †

- Patient diagnosis confirmed by elevated (age-adjusted) or equivocal serum IGF-1 as well as inadequate suppression of growth hormone (GH) after a glucose load; **AND**
- Patient has documented inadequate response to surgery and/or radiotherapy or it is not an option for the patient; **AND**
- Patient's tumor has been visualized on imaging studies (i.e., MRI or CT-scan); **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

- For Commercial and MMP members, the patient must have a documented failure, intolerance or contraindication to Sandostatin LAR (octreotide) or Somatuline Depot (lanreotide); OR
- For Medicaid members, the patient must have a documented failure, intolerance or contraindication to Somatuline Depot (lanreotide);

Cushing's Disease † Φ

- Confirmed diagnosis of endogenous Cushing's disease in which the patient's hypercortisolism is not a result of chronic administration of high-dose glucocorticoids or other physiologic conditions; **AND**
- Treatment of patient's disease with pituitary surgery has not been curative OR the patient 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:

- Patient 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) by random testing to < 1.0 mcg/L; **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 patients 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 patients 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; January 2023. Accessed November 2023.
2. Colao A, Bronstein MD, Freda P, et al. Pasireotide versus octreotide in acromegaly: a head-to-head superiority study. J Clin Endocrinol Metab. 2014 Mar; 99(3):791-9. doi: 10.1210/jc.2013-2480. Epub 2014 Jan 13.
3. Gadelha MR, Bronstein MD, Brue T, et al. Pasireotide versus continued treatment with octreotide or lanreotide in patients with inadequately controlled acromegaly (PAOLA): a randomised, phase 3 trial. Lancet Diabetes Endocrinol. 2014 Nov; 2(11):875-84. doi: 10.1016/S2213-8587(14)70169-X. Epub 2014 Sep 24.
4. Giustina A, Chanson P, Kleinberg D, et al. Expert consensus document: A consensus on the medical treatment of acromegaly. Nat Rev Endocrinol. 2014 Apr; 10(4):243-8. doi: 10.1038/nrendo.2014.21. Epub 2014 Feb 25.
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6. Lacroix A, Gu F, Gallardo W, Pivonello R, Yu Y, Witek P, Boscaro M, Salvatori R, Yamada M, Tauchmanova L, Roughton M, Ravichandran S, Petersenn S, Biller BMK, Newell-Price J; Pasireotide G2304 Study Group. Efficacy and safety of once-monthly pasireotide in Cushing's disease: a 12 month clinical trial. Lancet Diabetes Endocrinol. 2018 Jan;6(1):17-26. doi: 10.1016/S2213-8587(17)30326-1. Epub 2017 Oct 12. Erratum in: Lancet Diabetes Endocrinol. 2018 Jan;6(1):e1.
7. Biller BM, Grossman AB, Stewart PM, et al. Treatment of Adrenocorticotropin-Dependent Cushing's Syndrome: A Consensus Statement. J Clin Endocrinol Metab. July 2008, 93(7):2454-2462.
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 INTEGRITY (Medicare-Medicaid Plan) 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.