Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Pasireotide (Signifor®, Singnifor LAR®)	MP-RX-FP-134-24	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of *Pasireotide (Signifor®, Singnifor LAR®),* a somatostatin analog, approved by the Food and Drug Administration (FDA) for the treatment of patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

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.

Background Information

Pasireotide is a somatostatin analog that binds to somatostatin receptors (SSTRs) and have pharmacologic properties mimicking those of the natural hormone somatostatin. Signifor LAR is a long-acting release pasireotide agent. Signifor LAR must be administered by a healthcare professional by intramuscular injection and never administered intravenously. Pasireotide can cause increases in blood glucose levels which are sometimes severe.

Cushing's disease (CD)

Is the most common cause of Cushing's syndrome (CS) and is caused by an adrenocorticotropin (ACTH)-secreting pituitary benign tumor called adenoma. In this disease, the pituitary gland releases too much adrenocorticotropic hormone (ACTH) which stimulates the production and release of cortisol. The estimated incidence is 1 to 2 cases per million people per year with adult women more commonly affected than men. The long-term quality of life of the patients with CD is worse compared to other causes of Cushing's syndrome.

The diagnosis of CD includes clinical evaluation, hormone level measurements and imaging studies, such as MRI. The primary treatment for CS is surgical removal of the pituitary adenoma. In cases where surgery is not possible or is not curative, medication therapy with drugs that inhibits cortisol production, and radiation therapy can be considered.

Acromegaly

Is a rare disorder characterized by an excessive secretion of growth hormone (GH), leading to an overproduction of insulin-like growth factor 1 (IGF-1) and resulting in excessive growth of bones and body tissues, and other metabolic dysfunctions. The primary cause is usually a benign tumor of the pituitary gland. Its most often

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diagnosed in middle-aged adults, but symptoms can appear at any age. Complications may include cardiovascular diseases, diabetes mellitus, sleep apnea, and an increased risk of certain tumors.

The diagnosis of acromegaly involves clinical assessment, biochemical testing, and imaging studies, such as MRI. As with Cushing's disease, the primary treatment is surgical removal of the pituitary adenoma. In cases where surgery is not possible or is not curative, radiation therapy and medication therapy can be considered. Medications include somatostatin analogs, dopamine receptor agonists, GH-receptor antagonists or combination therapy.

Approved Indications

A. Treatment of patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative (Signifor, Signifor LAR).
B. Treatment of patients with acromegaly who have had an inadequate response to surgery and/or for whom surgery is not an option (Signifor LAR).

Other Uses

i. None.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J3490	Unclassified drugs (when specified as [Signifor] (pasireotide))
J3590	Unclassified biologics (when specified as [Signifor] (pasireotide))
J2502	Injection, pasireotide long acting, 1 mg [Signifor LAR]

ICD-10	Description
E24.0-E24.9	Cushing's Syndrome
E22.0	Acromegaly and pituitary gigantism

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Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Pasireotide (Signifor®, Singnifor LAR®)

A. Criteria For Initial Approval *(Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

Signifor®

i. Documentation is provided that individual has a diagnosis of Cushing's disease; **AND**
ii. Diagnosis of Cushing's has been verified by, or in consultation with, a board-certified endocrinologist who has reviewed and verified the test results (including but not limited to: 24-hour urinary free cortisol (UFC) test; Dexamethasone suppression test (DST); Late-night salivary cortisol (LNSC) test) that are indicative of a positive test; **AND**
iii. One of the following:
    A. Disease persists or recurs following pituitary surgery;
    OR
    B. Pituitary surgery is not indicated or an option.

Signifor LAR®

iv. Documentation is provided that individual has a diagnosis of acromegaly; **AND**
v. Diagnosis of acromegaly has been verified by, or in consultation with, a board-certified endocrinologist who has reviewed and verified the test results (including but not limited to: Insulin-like Growth Factor 1 levels; Oral Glucose Tolerance Test with associated Growth Hormone (GH) levels) that are indicative of a positive test; **AND**
vi. Individual has had an inadequate response to surgery and/or surgery is not an option (including but not limited to, individual is an inappropriate candidate for surgical-based therapy).

OR

vii. Documentation is provided that individual has a diagnosis of Cushing's disease; **AND**
viii. Diagnosis of Cushing's has been verified by, or in consultation with, a board-certified endocrinologist who has reviewed and verified the test results (including but not limited to: 24-hour urinary free cortisol (UFC) test; Dexamethasone suppression test (DST); Late-night salivary cortisol (LNSC) test) that are indicative of a positive test; **AND**
ix. One of the following:
    A. Disease persists or recurs following pituitary surgery;
    OR
    B. Pituitary surgery is not indicated or an option.

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B. Criteria For Continuation of Therapy

i. MMM considers continuation of Pasireotide (Signifor®, Singnifor LAR®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when if the following information is provided:
   A. Documentation of the patient's response to treatment showing no progression of disease.
   B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. Authorization Duration

i. Initial Approval Duration: Up to 12 months
ii. Reauthorization Approval Duration: Up to 12 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Signifor, Signifor LAR (pasireotide pamoate) may not be approved for the following:

   A. Individual has a diagnosis of severe hepatic impairment (Child Pugh C);
   OR
   B. When the above criteria are not met and for all other indications.

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

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B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug name	Indication	Dosage	Dosage in Hepatic Impairment
Pasireotide (Signifor ®) inj 0.3 mg/mL, 0.6 mg/mL, and 0.9 mg/mL in a SD ampule	Cushing's disease (CD)	• Initial dose: 0.6 mg or 0.9 mg SC twice a day • Recommended dosing range: 0.3 mg to 0.9 mg SC twice a day	• Child Pugh B: initial dosage is 0.3 mg twice a day and maximum dosage is 0.6 mg twice a day • Child Pugh C: Avoid use in these patients
Pasireotide (Signifor LAR ®) inj suspension 10 mg, 20 mg, 30 mg, 40 mg, and 60 mg vial	Cushing's disease (CD)	• Initial dose: is 10 mg IM once every 4 weeks (every 28 days) • Max dose: 40 mg once every 28 days	• Child Pugh B: initial dosage is 10 mg every 4 weeks and maximum dosage is 20 mg every 4 weeks • Child Pugh C: Avoid use in these patients
	Acromegaly	• Initial dose: is 40 mg IM once every 4 weeks (every 28 days) • Max dose: 60 mg once every 28 days	• Child Pugh B: initial dosage is 20 mg every 4 weeks and maximum dosage is 40 mg every 4 weeks • Child Pugh C: Avoid use in these patients

Exceptions

- Evaluate fasting plasma glucose (FPG), hemoglobin A1c (HbA1c), liver enzyme tests, electrocardiogram (ECG), serum magnesium, and serum potassium prior to starting.
  - Optimize glucose control in patients with poorly controlled diabetes mellitus prior to starting.
- Adjust dose based on response and tolerability.
- New onset steatorrhea, stool discoloration, loose stools, abdominal bloating, and weight loss may occur. If new occurrence or worsening of these symptoms are reported, evaluate for potential pancreatic exocrine insufficiency.

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Reference Information

1. Lancet Diabetes Endocrinol. 2021 December; 9(12): 847–875. Published online 2021 Oct 20. doi: 10.1016/S2213-8587(21)00235-7. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8743006/. Accessed on January 29, 2024.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: June 14, 2022.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review 12/24/2024	Updated background information to add pasireotide blood glucose increase and Signifor LAR information. Updated quantity limits table to add dosage form and strength for each drug and warnings and precautions based on recent FDA label changes. Minor wording and formatting changes. Coding reviewed: added J3490 and J3590 for Signifor.	3/20/2025	4/2/2025
Policy Inception 01/29/2024	Elevance Health's Medical Policy Adoption	N/A	6/28/2024