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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 02/08/2024

Somatostatin Analogs

Signifor[®] LAR (pasireotide)

HCPCS: J2502

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. FDA approved age
 - b. Diagnosis of one of the following:
 - i. Acromegaly in patients who have had an inadequate response to surgery and/or for whom surgery is not an option, and supported by an elevated Insulin-like Growth Factor-1 (IGF-1) level
 - ii. Cushing's Disease for whom pituitary surgery is not an option or has not been curative and the following:
 - a) Treatment failure to ketoconazole, mitotane or cabergoline, unless contraindicated or not tolerated
 - b) Treatment failure with Signifor. Please provide a credible explanation why Signifor LAR is expected to work if Signifor has not
 - c. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy documents.
- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity Limits: Align with FDA recommended dosing
 - b. Authorization Period: One year at a time
 - c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

Background Information:

- Lanreotide (Somatuline Depot®), octreotide (Sandostatin®, Sandostatin® LAR Depot), and pasireotide (Signifor, Signifor LAR®) are somatostatin analogs (SSAs). They have similar pharmacologic activity as the natural hormone, somatostatin. SSAs inhibit insulin, glucagon, and growth hormone (GH). They also suppress luteinizing hormone response to gonadotropin-releasing hormone, decrease splanchnic blood flow, and inhibit release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin, and pancreatic polypeptide. SSAs are approved for a number of conditions, including acromegaly, various neuroendocrine tumors (NETs) and their related symptoms, Cushing's disease, and carcinoid syndrome. Refer to the prescribing information for FDA approved indications for each product.
- Acromegaly is a disorder characterized by GH hypersecretion, multisystem associated morbidities, and increased mortality. The Acromegaly Consensus Group consensus statement on acromegaly therapeutic outcomes (2018) recommends surgical resection of the pituitary adenoma where possible as it represents the best opportunity for cure. For patients with persistent disease after surgery or in whom surgery is inappropriate, medical therapy is recommended.
 - A first-generation long-acting SSA (i.e., octreotide LAR, lanreotide) is recommended first-line for patients with significant disease that require medical therapy, while those with only mild signs and symptoms and modest IGF-1 elevation are recommended cabergoline.
 - Both octreotide LAR and lanreotide have similar efficacy rates; neither product is recommended over the other. Additional octreotide formulations approved for patients with acromegaly include short-acting injectable octreotide (Sandostatin) and an oral capsule (Mycapssa) indicated for patients already established on treatment with injectable octreotide or lanreotide. Of the available octreotide formulations, Sandostatin provides the greatest value since it is available as a generic and provides a cost-effective alternative to the branded octreotide products.
 - Efficacy can be judged by improvement in manifestations of acromegaly, such as decrease in GH and/or IGF-1 levels and/or decrease in pituitary tumor size.
 - If only a partial response is attained from first-generation SSA therapy, dose and/or frequency of the SSA may be increased or cabergoline can be added. If, however, SSA treatment generates minimal or no response, a switch to pasireotide LAR (Signifor LAR) should be considered. Pasireotide is a newer SSA with side effects similar to octreotide and lanreotide with the exception of hyperglycemia, which occurs in roughly 57% of patients. Given the prevalence of hyperglycemia, patients with impaired glucose metabolism who failed to respond to a first-generation SSA may require either a switch to pegvisomant (Somavert) or the addition of pegvisomant to SSA therapy depending on patient presentation.
- Cushing's disease (CD) is a rare disorder of chronic hypercortisolism due to corticotropin-secreting pituitary adenoma. Chronic hypercortisolism is associated with increased incidence of systemic arterial hypertension, diabetes mellitus, central obesity, hyperlipidemia and hypercoagulability.
 - The 2015 Endocrine Society clinical practice guideline for the treatment of Cushing's syndrome and the 2021 Pituitary Society consensus on diagnosis and management of Cushing's disease: a guideline update recommend that first-line treatment be the removal of the tumor unless surgery is not possible or unlikely to address the excess cortisol. If surgery is noncurative or not possible, second line treatment options include repeat TSS, radiotherapy, bilateral adrenalectomy, and medical therapy with steroidogenesis inhibitors, pituitary-directed treatments, or a glucocorticoid antagonist. The choice of second line treatment must be individualized to each patient based on the clinical scenario.

- Steroidogenesis inhibitors include ketoconazole, metyrapone, mitotane, and etomidate, and may be given as monotherapy or in combination with radiation therapy or radiosurgery. Pituitary-directed medical treatments include cabergoline and pasireotide. Pasireotide (Signifor® and Signifor® LAR) is FDA approved for the treatment of patients with Cushing's disease who are not surgical candidates or have failed surgery. The guidelines do not recommend the use of one medical therapy over another as second-line treatment after surgery or for those in whom surgery is not an option.
- Signs of treatment efficacy and clinical benefit include improvement in CD manifestations and normalization of urinary free cortisol from baseline.

References:

1. Katznelson L, Laws ER Jr, Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2014; 99:3933.
2. Nieman LK, Biller B, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2015;100:2807-2831.
3. Melmed, S., Bronstein, M.D., Chanson, P. et al. A Consensus Statement on acromegaly therapeutic outcomes. *Nat Rev Endocrinol* 14, 552–561 (2018). <https://doi.org/10.1038/s41574-018-0058-5>.
4. Lanreotide [prescribing information]. Warren, NJ; Cipla USA Inc.: December 2021.
5. Sandostatin® [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2018.
6. Sandostatin® LAR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2018.
7. Signifor® LAR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; January 2019.
8. Somatuline® Depot [package insert] Basking Ridge, NJ 07920. Ipsen Pharma Biotech; June 2019.
9. Fleseriu M, Auchus R, et al. Consensus on diagnosis and management of Cushing's disease: a guideline update. *Lancet Diabetes Endocrinol* 2021; 9: 847-75.

Policy History		
#	Date	Change Description
2.1	Effective Date: 02/08/2024	Removed Sandostatin LAR, Lanreotide, and Somatuline Depot from policy; no longer managed with PA.
2.0	Effective Date: 02/02/2023	Annual review of criteria was performed, no changes were made
1.9	Effective Date: 02/10/2022	Addition of Lanreotide SC and related criteria to the policy Addition of Signifor and related criteria to the policy; Signifor stand-alone policy will be retired. Removal of Sandostatin from the policy; no longer managed Removal of Bynfezia and related criteria from the policy; discontinued May 2021 Criteria updates as follows: <ul style="list-style-type: none"> - Removal of prescriber requirement - Removal of criteria regarding off-label use - Revised renewal criteria
1.8	Effective Date: 04/08/2021	Annual review of criteria was performed, no changes were made
1.7	Effective Date: 04/16/2020	Updated to include Bynfezia for pharmacy benefit
1.6	Effective Date: 05/09/2019	Updated trial and failure of preferred product verbiage for all products
1.5	Effective Date: 11/01/2018	New indication of Cushing's disease added
1.4	Effective Date: 05/03/2018	Updated with new Somatuline Depot indication presented at CCG
1.3	Effective Date: 02/09/2018	Annual review of criteria was performed, no changes were made
1.2	Effective Date: 02/08/2017	Annual review of criteria was performed, no changes were made
1.1	Effective Date: 01/01/2016	Document updated with specified drugs required
1.0	Effective Date: 09/21/2015	Class Document Development UM medical management system update for BCBS for Signifor LAR

* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Signifor® LAR (pasireotide) HCPCS CODE: J2502



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This form is to be used by participating physicians to obtain coverage for Signifor LAR. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	Name
ID Number	Specialty
D.O.B. <input type="checkbox"/> Male <input type="checkbox"/> Female Pt weight (in kg) Date recorded: _____	Address
Diagnosis	City /State/Zip
Drug Name	Phone/Fax: P: () - F: () -
Dose and Quantity	NPI
Directions	Contact Person
Date of Service(s)	Contact Person Phone / Ext.

STEP 1: DISEASE STATE INFORMATION

- Is this medication being administered by: Self (patient) Health care professional (physician/nurse)
- Is the patient being seen by an Endocrinologist? yes no Specialty: _____
- What is the patient's dose and frequency of requested therapy? _____
- Is this request for: Initiation Continuation **Original start date:** _____
- Initiation AND Continuation of therapy:**
 - Please check the patient's diagnosis: Acromegaly Cushings Disease
 Hormone secreting tumors of the GI tract Other: _____
 - Has the patient had a poor response to surgery and/or is surgery not an option for them?
 yes no; Please explain: _____
 - Does the patient have elevated insulin-like growth factor-1 (IGF-1)? (*Before treatment started*)
 yes, current level _____, date drawn: _____ no
 - Please check which medications the patient has tried:
 Somatuline Depot Sandostatin
 Sandostatin LAR Somavert Other: _____
- Continuation request:** Signifor LAR start date: _____
 - Has the patient had improvement in manifestations of acromegaly?
 yes no; Please explain: _____
 - If the patient has improvement in manifestations of acromegaly, please check which apply:
 Decrease in Growth Hormone (GH) and/or IGF-1 levels
 Decrease in pituitary tumor size
 Other, explain: _____
- Please attach any chart notes or additional documentation and submit to plan. (**Required**)

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
Step 2: Checklist	<input type="checkbox"/> Form Completely Filled Out <input type="checkbox"/> Attached Chart Notes	<input type="checkbox"/> Patient and Physician Information complete
Step 3: Submit	By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979	By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320

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