Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

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: 12/12/2024

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 indication
   b. FDA approved age
   c. For a diagnosis of acromegaly:
      i. Diagnosis is supported by an elevated Insulin-like Growth Factor-1 (IGF-1) level
   d. For a diagnosis of Cushing's disease:
      i. Trial and failure of ketoconazole, mitotane or cabergoline, unless contraindicated or not tolerated
      ii. Trial and failure of Signifor. Please provide a credible explanation why Signifor LAR is expected to work if Signifor has not
   e. 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.

Background Information:

- Lanreotide (Somatuline Depot®), octreotide (Sandostatin®, Sandostatin® LAR Depot, Bynfezia Pen), 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 multidisciplinary management of acromegaly (2020) recommends surgical resection of the pituitary adenoma via transsphenoidal surgery where possible as it is safe and effective represents the best opportunity for cure. IGF-1 levels reflect clinical activity of disease, and levels assessed at least 3 months post-operatively can reliably define remission.

- For patients with persistent disease who do not achieve biochemical control after surgery or in whom surgery is inappropriate, medical therapy is recommended. Choice of therapy is recommended to be individualized based on disease- and patient-specific factors that may affect therapeutic efficacy and safety.

    - 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, Bynfezia Pen) and an oral capsule (Mycapssa). Bynfezia Pen is a multi-dose, prefilled pen formulation of octreotide intended for self-administration via subcutaneous injection, and Mycapssa is indicated for long-term maintenance treatment in acromegaly patients who have already responded to and tolerated treatment with octreotide or lanreotide.

        - Of the available octreotide formulations, Sandostatin provides the greatest value since it is available as a generic in single- and multi-dose vials as well as single-dose prefilled syringes 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, if at maximal doses of SSA therapy, cabergoline can be added. If, however, SSA treatment generates minimal or no response, a switch to pasireotide LAR (Signifor LAR) may be considered as it can be effective in normalizing IGF-1 levels in some patients that are not adequately controlled by octreotide LAR or lanreotide and may produce a higher rate of tumor shrinkage.

    - 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. Pegvisomant is generally used as second-line therapy in patients unable to achieve biochemical control with maximal doses of SSA.

- 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. Giustina, A., Barkhoudarian, G., Beckers, A. et al. Multidisciplinary management of acromegaly: A consensus. Rev Endocr Metab Disord 21, 667–678 (2020). https://doi.org/10.1007/s11154-020-09588-z
2. Katznelson L, Laws ER Jr, Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2014; 99:3933.
3. 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.
4. 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.
5. 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.
6. Lanreotide [prescribing information]. Warren, NJ; Cipla USA Inc.: December 2021.
7. Sandostatin [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2018.
8. Sandostatin LAR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2018.
9. Signifor LAR [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; January 2019.
10. Somatuline Depot [package insert] Basking Ridge, NJ 07920. Ipsen Pharma Biotech; June 2019.
11. Bynfezia Pen [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc,; September 2024.
12. Mycapssa [prescribing information]. Scotland, UK: Chiasma; June 2020

Policy History		
#	Date	Change Description
2.2	Effective Date: 12/12/2024	Added Mycapssa and Bynfezia Pen and listed FDA approved indications instead of listing all the indications out individually
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: - 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. ☐Male ☐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

1. Is this medication being administered by: ☐ Self (patient) ☐ Health care professional (physician/nurse)
2. Is the patient being seen by an Endocrinologist? ☐ yes ☐ no Specialty: _____
3. What is the patient's dose and frequency of requested therapy? _____
4. Is this request for: ☐ Initiation ☐ Continuation ***Original start date:*** _____
5. **Initiation AND Continuation of therapy:**
   a. Please check the patient's diagnosis: ☐ Acromegaly ☐ Cushings Disease
      ☐ Hormone secreting tumors of the GI tract ☐ Other: _____
   b. Has the patient had a poor response to surgery and/or is surgery not an option for them?
      ☐ yes ☐ no; Please explain: _____
   c. Does the patient have elevated insulin-like growth factor-1 (IGF-1)? *(Before treatment started)*
      ☐ yes, current level _____, date drawn: _____ ☐ no
   d. Please check which medications the patient has tried:
      ☐ Somatuline Depot ☐ Sandostatin
      ☐ Sandostatin LAR ☐ Somavert ☐ Other: _____
6. **Continuation request:** Signifor LAR start date: _____
   a. Has the patient had improvement in manifestations of acromegaly?
      ☐ yes ☐ no; Please explain: _____
   b. 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: _____
7. 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	☐ Form Completely Filled Out ☐ Attached Chart Notes	☐ 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**

9/22/2015; 11/20/2015; 2/2/2018;10/11/2018