MEDICAL MUTUAL®

Drug Policy

Policy:	Signifor LAR (pasireotide)	Annual Review Date: 11/16/2023 Last Revised Date: 11/16/2023

OVERVIEW

Signifor LAR is a 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 and for patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative. This medication has also been used to treat metastatic neuroendocrine tumors (NETs) in the gastrointestinal tract. Signifor LAR is a long-acting release form of pasireotide, which binds to somatostatin receptors (SSTRs) and has pharmacologic properties mimicking those of the natural hormone somatostatin.

POLICY STATEMENT

This policy involves the use of Signifor LAR. Prior authorization is recommended for pharmacy benefit coverage of Signifor LAR. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Signifor LAR as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Signifor LAR be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Signifor LAR is recommended in those who meet the following criteria:

1. **Acromegaly**
   Criteria. *Patient must meet the following criteria*
   - **A.** The medication is prescribed by or in consultation with an endocrinologist; AND
   - **B.** The patient has had an inadequate response to or is ineligible for surgery OR is experiencing negative effects due to tumor size (e.g. optic nerve compression); AND
   - **C.** The patient had a baseline (prior to initiation of any somatostatin analog [Signifor LAR, Somatuline Depot, Sandostatin LAR], dopamine agonist [bromocriptine, cabergoline] or Somavert) IGF-1 level above the upper limit of normal (ULN) for age and gender per the laboratory's standard reference values; AND
   - **D.** The patient has failed on an adequate trial of Somatuline Depot

2. Cushing's Syndrome
Criteria. *Patient must meet the following criteria*

A. This medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of Cushing's Syndrome; AND
B. The patient has had an inadequate response to or is ineligible for pituitary surgery OR is awaiting surgery or therapeutic response after radiotherapy.

3. Refractory Carcinoid Syndrome- Neuroendocrine Tumors (NETs) of the GI Tract
Criteria. *Patient must meet the following criteria*

A. The medication is prescribed by or in consultation with an endocrinologist, gastroenterologist, or oncologist; AND
B. The patient has metastatic NETs of the GIT; AND
C. The patient has been inadequately controlled using first generation somatostatin analogs (e.g. Sandostatin LAR)

Initial Approval/ Extended Approval.
A) *Initial Approval:* Acromegaly: 1 year; Cushing's Syndrome: 4 months
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Signifor LAR has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Signifor® LAR injectable suspension [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2018.
2. Giustina A, Chanson P, Kleinberg D, et al. A consensus on the medical treatment of acromegaly. *Nat Rev Endocrinol.* 2014;10(4):243-248.
3. Katznelson L, Laws ER Jr, Melmed S, et al; Endocrine Society. Acromegaly: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99:3933-3951.
4. Melmed S. Acromegaly. *N Engl J Med*. 2006;355:2558-2573.
5. Christofides EA. Clinical importance of achieving biochemical control with medical therapy in adult patients with acromegaly. *Patient Pref Adherence*. 2016;10:1217-1225.
6. Oberg K, Lamberts SW. Somatostatin analogues in acromegaly and gastroenteropancreatic neuroendocrine tumours: past, present and future. *Endocr Relat Cancer*. 2016;23(12):R551-566.
7. Manjila S, Wu OC, Khan FR, et al. Pharmacological management of acromegaly: a current perspective. *Neurosurg Focus*. 2010;29(4):E14.
8. Colao A, Bronstein MD, Freda P, et al. Pasireotide versus octreotide in acromegaly: a head-to-head superiority study. *J Clin Endocrinol Metab*. 2014;99(3):791-799.
9. Gadelha MR, Bronstein MD, Brue T, et al. Pasireotide versus continued treatment with octreotide or lanreotide in patients with inadequately controlled acromegaly (PAOLA): a randomized, phase 3 trial. *Lancet Diabetes Endocrinol*. 2014;2(11):875-884.
10. Sheppard M, Bronstein MD, Freda P, et al. Pasireotide LAR maintains inhibition of GH and IGF-1 in patients with acromegaly for up to 25 months: results from the blinded extension phase of a randomized, double-blind, multicenter, Phase III study. *Pituitary*. 2015;18(3):385-394.
11. Novartis. Efficacy and safety of pasireotide administered monthly in patients with Cushing's Disease. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2015 Jan 26]. Available from: https://www.clinicaltrials.gov/ct2/show/NCT01374906?term=pasireotide+and+cushing%27s&rank=1 NLM Identifier: NCT01374906.
12. Tritos NA, Biller BM. Advances in medical therapies for Cushing's syndrome. *Discov Med*. 2012;13(69):171-179.
13. Biller BMK, Grossman AB, Stewart PM, et al. Treatment of adrenocorticotropin-dependent Cushing's syndrome: A consensus statement. *J Clin Endocrinol Metab*. 2008;93:2454-2462.
14. Arnaldi G and Boscaro M. New treatment guidelines on Cushing's disease. *F1000 Med Rep*. 2009;1.
15. Mazziotti G, Gazzaruso C and Giustina A. Diabetes in Cushing syndrome: basic and clinical aspects. *Trends Endocrinol Metab*. 2011;22(12):499-506.
16. Rizk A, Honegger J, Milian M and Psaras T. Treatment options in Cushing's disease. *Clin Med Insights Oncol*. 2012(6):75-84.
17. Pasireotide. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 6 September 2019. Accessed on 18 November 2019.
18. Pavel M, O'Toole D, Costa F, et al: ENETS consensus guidelines update for the management of distant metastatic disease of intestinal, pancreatic, bronchial neuroendocrine neoplasms (NEN) and NEN of unknown primary site. Neuroendocrinology 2016; 103(2):172-185.