

Clinical Policy: Pasireotide (Signifor, Signifor LAR)

Reference Number: ERX.SPA.212

Effective Date: 01.11.17

Last Review Date: 11.21

Line of Business: Commercial, Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

Description

Pasireotide (Signifor[®], Signifor[®] LAR) is a somatostatin analog.

FDA Approved Indication(s)

Signifor is indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

Signifor LAR is 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
- Cushing's disease for whom pituitary surgery is not an option or has not been curative

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions[™] that Signifor and Signifor LAR **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acromegaly (must meet all):

1. Diagnosis of acromegaly;
2. Prescribed by or in consultation with an endocrinologist;
3. Age \geq 18 years;
4. Request is for Signifor LAR;
5. Inadequate response to surgical resection or pituitary irradiation (see *Appendix D*), or member is not a candidate for such treatment;
6. Dose does not exceed 60 mg (1 vial) every 4 weeks.

Approval duration: 6 months

B. Cushing's Disease (must meet all):

1. Diagnosis of Cushing's disease;
2. Prescribed by or in consultation with an endocrinologist;
3. Age \geq 18 years;
4. Member meets one of the following (a or b):
 - a. Pituitary surgery was not curative;
 - b. Member is not eligible for pituitary surgery;
5. Dose does not exceed one of the following (a or b):
 - a. Signifor: 1.8 mg (2 ampules of 0.9 mg) per day;
 - b. Signifor LAR: 40 mg (1 vial) every 4 weeks.

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Acromegaly (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy (*see Appendix D*);
3. Request is for Signifor LAR;
4. If request is for a dose increase, new dose does not exceed 60 mg (1 vial) every 4 weeks.

Approval duration: 12 months

B. Cushing's Disease (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy (*see Appendix D*);
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
 - a. Signifor: 1.8 mg (2 ampules of 0.9mg) per day;
 - b. Signifor LAR: 40 mg (1 vial) every 4 weeks.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Treatment response for Cushing's disease may be defined as clinically meaningful reduction in 24-hour urinary free cortisol (UFC) levels and/or improvement in signs or symptoms of the disease. Maximum urinary free cortisol reduction is typically seen by two months of treatment.
- Examples of treatment response to acromegaly therapy (including somatostatin analogs, surgical resection or pituitary irradiation) include improvement from baseline in or normalization of growth hormone (GH) and/or age- and sex-adjusted insulin-like growth factor (IGF-1) serum concentrations, or tumor mass control.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Pasireotide (Signifor)	Cushing's disease	Initial: 0.6 mg or 0.9 mg SC BID	1.8 mg/day
Pasireotide (Signifor LAR)	Cushing's disease	10 mg to 40 mg IM every 4 weeks	40 mg/4 weeks
Pasireotide (Signifor LAR)	Acromegaly	40 mg to 60 mg IM every 4 weeks	60 mg/4 weeks

**Signifor LAR must be administered by a healthcare professional*

VI. Product Availability

Drug Name	Availability
Pasireotide (Signifor)	Single-dose ampules for injection: 0.3 mg/mL, 0.6 mg/mL, 0.9 mg/mL
Pasireotide (Signifor LAR)	Vial for reconstitution and injectable suspension: 10 mg, 20 mg, 30 mg, 40 mg, 60 mg

VII. References

1. Signifor Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2020. Available at: <https://www.signifor.com/pdf/signifor-pi.pdf>. Accessed August 12, 2021.
2. Signifor LAR Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2020. Available at: <https://www.signiforlar.com/pdf/signifor-lar-pi.pdf>. Accessed August 12, 2021.
3. Melmed S, Bronstein MD, Chanson P. A Consensus Statement on acromegaly therapeutic outcomes. *Nat Rev Endocrinol.* 2018 Sep;14(9):552-561. doi: 10.1038/s41574-018-0058-5. Available at: <https://www.nature.com/articles/s41574-018-0058-5>. Available at: <https://www.nature.com/articles/s41574-018-0058-5>
4. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2014; 99(11): 3933-3951.
5. Nieman LK, Biller BMK, Findling JW, et al. Treatment of Cushing's syndrome: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2015; 100(8): 2807-2831. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4525003/?report=printable>.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	12.16	01.17
4Q17 Annual Review Converted to new template. Added max dose to criteria. Added consultation with an endocrinologist, age ≥ 18 years, For Cushing's added requirement of pituitary surgery not curative or not eligible for pituitary surgery, per FDA indication. In continued therapy added examples of positive response and max doses.	09.22.17	11.17
4Q 2018 annual review: criteria added for new FDA indication for Signifor LAR: Cushing's disease; new strengths of Signifor LAR added; simplified max dose requirement of Signifor LAR for acromegaly; initial approval duration for acromegaly revised to 3 months to allow for dose adjustment; requirement for inadequate response to surgery or pituitary irradiation added for acromegaly; specific requirements for positive response to therapy for acromegaly moved to appendix; references reviewed and updated.	08.14.18	11.18
4Q 2019 annual review: increased acromegaly initial approval duration from 3 months to 6 months to align with approach for other acromegaly policies; references reviewed and updated.	08.27.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.11.20	11.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2021 annual review: no significant changes; references reviewed and updated.	8.25.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

This policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2017 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.