

**Title:** Cushing's Disease Agents

**Policy #:** Rx.01.132

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***Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.***

***This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.***

***Members are advised to use participating pharmacies in order to receive the highest level of benefits.***

**Intent:**

The intent of this policy is to communicate the medical necessity criteria for **pasireotide (Signifior®)**, **osilodrostat (Isturisa®)**, and **mifepristone (Korlym®)** as provided under the member's prescription drug benefit.

**Description:**

Cushing's disease is caused by an adrenocorticotrophic hormone (ACTH) secreting pituitary tumor. Surgical intervention is required for optimal treatment of Cushing's disease. When surgery is delayed, contraindicated, or unsuccessful, medical therapy may be required. Cabergoline and pasireotide are medications that target the tumor and may help normalize urinary free cortisol.

**Pasireotide (Signifior®)** exerts its pharmacological activity via binding to somatostatin receptors (SSTRs). Pasireotide binds and activates the SSTRs, resulting in inhibition of ACTH secretion, which leads to decreased cortisol secretion.

**Osilodrostat (Isturisa®)** is a cortisol synthesis inhibitor. It inhibits 11beta-hydroxylase (CYP11B1), the enzyme responsible for the final step of cortisol biosynthesis in the adrenal gland.

**Mifepristone (Korlym®)** is a selective antagonist of the progesterone receptor at low doses and blocks the glucocorticoid receptor (GR-II) at higher doses. Mifepristone has high affinity for the GR-II receptor but little affinity for the GR-I (MR, mineralocorticoid) receptor. In addition, mifepristone appears to have little or no affinity for estrogen, muscarinic, histaminic, or monoamine receptors.

**Pasireotide (Signifior®)** 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.

**Osilodrostat (Isturisa®)** 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.

**Mifepristone (Korlym®)** indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery.

**Policy:**

Pasireotide (Signifior®) is approved when ALL of the following inclusion criteria are met:

1. Diagnosis of Cushing's disease; and
2. Member has failed surgery or is not a candidate for surgery; and
3. Member is 18 years of age or older; and

4. Prescribed by or in consultation with an endocrinologist

Mifepristone (Korlym®) is approved when documentation is provided of ALL of the following:

1. Hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance; and
2. Member has failed surgery or is not a candidate for surgery; and
3. Prescribed by or in consultation with an endocrinologist

#### INITIAL CRITERIA

Osilodrostat (Isturisa®) is approved when ALL of the following are met:

1. Diagnosis of Cushing's disease; and
2. Member has failed surgery or is not a candidate for surgery; and
3. Member is 18 years of age or older; and
4. Prescribed by or in consultation with an endocrinologist; and
5. Member has inadequate response or inability to tolerate Signifor® [LAR]

Initial Authorization: 6 months

#### REAUTHORIZATION CRITERIA

Osilodrostat (Isturisa®) is approved when ALL of the following are met:

1. Member has positive response to therapy (i.e. cortisol levels in range, improved signs and symptoms); and
2. Prescribed by or in consultation with an endocrinologist

Reauthorization –12 months

#### **Black Box Warning as shown in the drug Prescribing Information:**

##### **Mifepristone (Korlym®)**

- TERMINATION OF PREGNANCY
  - Mifepristone is a potent antagonist of progesterone and cortisol via the progesterone and glucocorticoid (GR-II) receptors, respectively. The antiprogestational effects will result in the termination of pregnancy. Pregnancy must therefore be excluded before the initiation of treatment with KORLYM and prevented during treatment and for one month after stopping treatment by the use of a non-hormonal medically acceptable method of contraception unless the patient has had a surgical sterilization, in which case no additional contraception is needed. Pregnancy must also be excluded if treatment is interrupted for more than 14 days in females of reproductive potential.

#### **Guidelines:**

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

#### **BENEFIT APPLICATION**

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

#### **References:**

Nieman LK. Medical therapy of hypercortisolism (Cushing's syndrome). UpToDate. June 2020. Available at: [https://www.uptodate.com/contents/medical-therapy-of-hypercortisolism-cushings-syndrome?source=search\\_result&search=cushings%20disease&selectedTitle=8~100#H1](https://www.uptodate.com/contents/medical-therapy-of-hypercortisolism-cushings-syndrome?source=search_result&search=cushings%20disease&selectedTitle=8~100#H1). Accessed August 24, 2020.

Nieman LK. Overview of the treatment of Cushing's syndrome. UpToDate. October 2019. Available at: <https://www.uptodate.com/contents/overview-of-the-treatment-of-cushings->

[syndrome?source=search\\_result&search=cushings%20disease%20management&selectedTitle=1~100#H4](#). Accessed August 24, 2020.

Isturisa® (osilodrostat) [prescribing information]. Lebanon, NJ: Recordati Rare Disease, Inc.; March 2020. Available from: <https://www.isturisa.com/pdf/isturisa-prescribing-information.pdf>. Accessed August 24, 2020.

Korlym® (mifepristone) [prescribing information]. Menlo Park, CA: Corcept Therapeutics Inc.; November 2019. Available from: [https://www.korlym.com/wp-content/uploads/2018/01/K-00017-NOV-2019\\_electronic-PI\\_r8\\_FINAL.pdf](https://www.korlym.com/wp-content/uploads/2018/01/K-00017-NOV-2019_electronic-PI_r8_FINAL.pdf). Accessed August 24, 2020.

Signifor® (pasireotide) [package insert]. East Hanover, NJ. Novartis Pharmaceuticals Corporation. June 2020. Available at: <https://www.signiforlar.com/pdf/signifor-lar-pi.pdf>. Accessed August 24, 2020.

**Applicable Drugs:**

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

<b>Brand name</b>	<b>Generic name</b>
Signifor®	Pasireotide
Isturisa®	Osilodrostat
Korlym®	Mifepristone

**Cross References:**

Off-Label Use policy Rx.01.33

Quantity Level Limits for Pharmaceuticals Covered Under the Prescription Drug Benefit Rx.01.76

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<b>Policy Version Number:</b>	8.00
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<b>Policy Effective Date:</b>	October 01, 2020
<b>Next Required Review Date:</b>	January 09, 2021

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The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.

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