# Drug Coverage Policy

**Effective Date ..... 10/01/2025**
**Coverage Policy Number.....IP0044**
**Policy Title.....Isturisa**

# Cushing's – Isturisa

- Isturisa® (osilodrostat tablets – Recordati Rare Diseases)

***INSTRUCTIONS FOR USE***
*The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.*

**Overview**

Isturisa, a cortisol synthesis inhibitor, is indicated for the **treatment of endogenous hypercortisolemia** in adults with **Cushing's syndrome** for whom pituitary surgery is not an option or has not been curative.[1]

**Disease Overview**

Cushing's syndrome refers to the general state of excessive levels of cortisol (hypercortisolism) in the blood.[2,3] Hypercortisolism can occur for reasons that are either endogenous or exogenous in nature (e.g., Cushing's disease, cortisol-containing medications, adrenal gland tumor, certain cancers). Cushing's disease (hypercortisolism caused by pituitary adenomas) is the most common type of adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome. Treatment for Cushing's syndrome requires a multi-modal approach. The goals of treatment are normalization of cortisol excess, long-term disease control, avoidance of recurrence, and reversal of clinical features.[4]

**Guidelines**
The Endocrine Society published clinical practice guidelines (2015) for the treatment of Cushing's syndrome.[5] Isturisa is not addressed in the guidelines. First-line treatment involves resection of the tumor, unless surgery is not possible or is unlikely to meaningfully reduce excess glucocorticoid levels. In patients with ACTH-dependent Cushing's syndrome who underwent non-curative surgery or for whom surgery was not possible, the guidelines advocate several second-line therapies (e.g., repeat transsphenoidal surgery, radiotherapy, medical therapy, and bilateral adrenalectomy). For Cushing's disease, the guidelines recommend all medical therapies as second-line options after transsphenoidal surgery: steroidogenesis inhibitors (ketoconazole tablets, Metopirone® [metyrapone capsules], Lysodren® [mitotane tablets], etomidate injection) in patients either with or without radiotherapy/radiosurgery; pituitary-directed medical treatments (cabergoline tablets, Signifor® [pasireotide subcutaneous injection]) in patients who are not surgical candidates or who have persistent disease; and mifepristone tablets (Korlym®, generic) in patients with diabetes or glucose intolerance who are not surgical candidates or who have persistent disease after transsphenoidal surgery.

## Coverage Policy

**POLICY STATEMENT**
Prior Authorization is required for prescription benefit coverage of Isturisa. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Isturisa as well as the monitoring required for adverse events and long-term efficacy, approval requires Isturisa to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Documentation:** Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but not limited to, chart notes, laboratory tests, medical test results, claims records, and/or other information.

**Isturisa is considered medically necessary when the following is met:**

**FDA-Approved Indication**

1. **Endogenous Cushing's Syndrome.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   Note: Cushing's disease is included in endogenous Cushing's syndrome.
   - **A.** Patient is ≥ 18 years of age; AND
   - **B.** The patient has confirmed diagnosis of Endogenous Cushing's Syndrome **[Documentation Required]**; AND
     Note: Examples of documentation include a chart note, laboratory or medical test results, etc.
   - **C.** Patient meets ONE of the following (i, ii, or iii)

**i.** According to the prescriber, the patient is not a candidate for surgery or surgery has not been curative; OR
**ii.** Patient is awaiting surgery for endogenous Cushing's Syndrome; OR
**iii.** Patient is awaiting therapeutic response after radiotherapy for endogenous Cushing's Syndrome; AND

**D.** The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of endogenous Cushing's syndrome; AND
**E.** Preferred product criteria is met for the product(s) as listed in the below table(s)

**Employer Plans:**

| Product | Criteria |
|---|---|
| **Isturisa** (osilodrostat tablets) | Cushing's Disease in a patient ≥ 18 years of age.<br>Approve if the patient meets one of the following (A or B):<br>A. Patient has tried, or is currently taking, one of Signifor or Signifor LAR; OR<br>B. Patient has already been started on Isturisa.<br><br>Endogenous Cushing's Syndrome in a patient ≥ 18 years of age.<br>Note: This includes patients awaiting surgery and patients awaiting therapeutic response after pituitary radiotherapy.<br>Approve if the patient meets one of the following (A or B):<br>A. Patient has tried, and, according to the prescriber, the patient has had inadequate efficacy or significant intolerance to, or is currently taking, ONE of oral ketoconazole, Metopirone (metyrapone capsules), or Recorlev; OR<br>B. Patient has already been started on Isturisa. |

**Individual and Family Plans:**

| Product | Criteria |
|---|---|
| **Isturisa** (osilodrostat tablets) | Cushing's Disease in a patient ≥ 18 years of age.<br>Approve if the patient meets one of the following (A or B):<br>A. Patient has tried, or is currently taking, one of Signifor or Signifor LAR; OR<br>B. Patient has already been started on Isturisa.<br><br>Endogenous Cushing's Syndrome in a patient ≥ 18 years of age.<br>Note: This includes patients awaiting surgery and patients awaiting therapeutic response after pituitary radiotherapy.<br>A. The patient meets one of the following (A or B):<br>Patient has tried and, according to the prescriber, the patient has had inadequate efficacy or significant intolerance to, or is currently taking, one of oral ketoconazole, Metopirone [metyrapone capsules] (Requires Prior Authorization) or Recorlev (Requires Prior Authorization); OR<br>B. Patient has already been started on Isturisa. |

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

**Conditions Not Covered**

**Isturisa for any other use is not medically necessary. Criteria will be updated as new published data are available.**

## References


1. Isturisa® tablets [prescribing information]. Lebanon, NJ: Recordati Rare Diseases; April 2025.
2. Sharma ST, Nieman LK, Feelders RA. Cushing's syndrome: epidemiology and developments in disease management. *Clin Epidemiol*. 2015;7:281–293.
3. Tritos NA, Biller BM. Advances in medical therapies for Cushing's syndrome. *Discov Med*. 2012;13(69):171-179.
4. 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.
5. Nieman LK, Biller BM, Findling JW. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2015;100(8):2807-2831.


## Revision Details

| Type of Revision | Summary of Changes | Date |
|---|---|---|
| Annual Review | **Endogenous Cushing's Syndrome:** A patient who is awaiting surgery and a patient who is awaiting therapeutic response after radiotherapy were added as options of approval; for these conditions (patient who is awaiting surgery and a patient who is awaiting therapeutic response after radiotherapy) a requirement was added that the patient has tried one other medication or the patient is currently receiving Isturisa were added.<br>**Endogenous Cushing's Syndrome – Patient Awaiting Surgery:** This condition was removed from the policy and is now addressed under Endogenous Cushing's Syndrome.<br>**Endogenous Cushing's Syndrome – Patient Awaiting Therapeutic Response After Radiotherapy:** This condition was removed from the policy and is now addressed under Endogenous Cushing's Syndrome. | 08/01/2024 |
| Annual Review | **Endogenous Cushing's Syndrome:** This condition was moved from "other uses with supportive evidence" to "FDA-approved indication". Removed criterion for trial of previous therapies.<br>**Cushing's Disease:** This condition was removed from the policy as it is no longer an FDA approved indication and falls under the broader term, Cushing's Syndrome.<br>**Added** a requirement for a patient to have a documented diagnosis of Cushing's syndrome.<br>**Removed** prerequisite step for Endogenous Cushing's Syndrome. | 08/01/2025 |

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|---|---|---|
| | **Updated** the Employer Plans preferred product requirements.<br>**Added** Individual and Family Plans preferred product requirements.<br>**Reworded** the conditions not covered statement. | |
| Selected Revision | **Updated** the diagnostic requirement by removing "According to the prescriber". | 10/01/2025 |

The policy effective date is in force until updated or retired.