PRIOR AUTHORIZATION POLICY

POLICY: Cushing's – Isturisa Prior Authorization Policy
- Isturisa® (osilodrostat tablets – Recordati Rare Diseases)

REVIEW DATE: 04/19/2024

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 AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. 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.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Isturisa, a cortisol synthesis inhibitor, is indicated for the treatment of **Cushing's disease** in adults 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.

POLICY STATEMENT

Prior Authorization is recommended 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.

- **Isturisa® (osilodrostat tablets – Recordati Rare Diseases)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Cushing's Disease.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** According to the prescriber, the patient is not a candidate for surgery or surgery has not been curative; AND
     Note: For a patient with endogenous Cushing's syndrome awaiting surgery or therapeutic response after radiotherapy, see *Other Uses with Supportive Evidence*.
   - **C)** The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of Cushing's disease.

Other Uses with Supportive Evidence

2. **Endogenous Cushing's Syndrome.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** 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
   - **C)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has tried one of ketoconazole tablets, mifepristone tablets (Korlym, generic), Metopirone (metyrapone capsules), Lysodren (mitotane tablets), Signifor (pasireotide subcutaneous injection), or Signifor LAR (pasireotide intramuscular injection) for the treatment of endogenous Cushing's syndrome; OR
     - **ii.** Patient is currently receiving Isturisa; 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.

CONDITIONS NOT COVERED

- **Isturisa® (osilodrostat tablets – Recordati Rare Diseases)**

is(are) considered experimental, investigational, or unproven for ANY other use(s).

REFERENCES

1. Isturisa® tablets [prescribing information]. Lebanon, NJ: Recordati Rare Diseases; November 2023.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria change.	06/14/2023
Early Annual Revision	**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. **Endogenous Cushing's Syndrome – Patient Awaiting Surgery:** This condition was removed from the policy and is now addressed under Endogenous Cushing's Syndrome. **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.	04/19/2024