Effective Date **12/1/2023**
Next Review Date… **12/1/2024**
Coverage Policy Number **IP0044**

Osilodrostat

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Related Coverage Resources

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. 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

This policy supports medical necessity review for osilodrostat (**Isturisa®**).

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

Medical Necessity Criteria

Osilodrostat (Isturisa) is considered medically necessary when ONE of the following is met (1, 2, 3 or 4):

1. **Cushing's Disease.** Individual meets **ALL** of the following criteria:
   A. Age 18 years or older
   B. The individual is not a candidate for surgery or surgery has not been curative
   C. The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of Cushing's disease.
   D. Individual meets the preferred covered alternative(s) criteria as indicated in the table below

Coverage requires the use of preferred products. Refer to the customer's benefit plan document for coverage details.

Employer Group Non-Covered Products and Preferred Covered Alternatives:

Non-Covered Product	Criteria
Isturisa (osilodrostat tablets)	For Cushing's disease only, individual meets **ONE** of the following (A or B): A. Documented inadequate response, contraindication, or intolerance to **ONE** of the following: i. Signifor (pasireotide injection) [requires prior authorization] ii. Signifor LAR (pasireotide injection) [requires prior authorization] B. Individual is currently receiving Isturisa

2. **Endogenous Cushing's Syndrome.** Individual meets **ALL** of the following criteria:
   A. Age 18 years or older
   B. The individual is not a candidate for surgery or surgery has not been curative
   C. Documentation of **ONE** of the following (i, ii, or iii):
      i. Inadequate response to **ONE** of the following:
         a. ketoconazole tablets
         b. Korlym (mifepristone tablets) [requires prior authorization]
         c. Metopirone (metyrapone capsules)
         d. Lysodren (mitotane tablets)
         e. Signifor (pasireotide subcutaneous injection) [requires prior authorization]
         f. Signifor LAR (pasireotide intramuscular injection) [requires prior authorization]
      ii. Contraindication or intolerance to **ALL** of the following:
         a. Korlym (mifepristone tablets) [requires prior authorization]
         b. Signifor (pasireotide subcutaneous injection) [requires prior authorization]
         c. Signifor LAR (pasireotide intramuscular injection) [requires prior authorization]
      iii. Individual is currently receiving Isturisa
   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

3. **Endogenous Cushing's Syndrome – Individuals Awaiting Surgery.** Individual meets **BOTH** of the following criteria:
   A. Age 18 years or older
   B. The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of endogenous Cushing's syndrome.

4. **Endogenous Cushing's Syndrome – Individuals Awaiting Therapeutic Response After Radiotherapy.** Individual meets **BOTH** of the following criteria:
   A. Age 18 years or older
   B. The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of endogenous Cushing's syndrome.

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.

Reauthorization Criteria

Osilodrostat (Isturisa) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial and reauthorization approval duration:

- Cushing's Disease: up to 1 year
- Endogenous Cushing's Syndrome: up to 1 year
- Endogenous Cushing's Syndrome – Individuals Awaiting Surgery: up to 6 months
- Endogenous Cushing's Syndrome – Individuals Awaiting Therapeutic Response After Radiotherapy: up to 6 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

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 Korlym® (mifepristone tablets) in patients with diabetes or glucose intolerance who are not surgical candidates or who have persistent disease after transsphenoidal surgery.

References

1. Isturisa® tablets [prescribing information]. Lebanon, NJ: Recordati Rare Diseases; March 2020.
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.