

## Clinical Policy: Osilodrostat (Isturisa)

Reference Number: ERX.SPA.396

Effective Date: 09.01.20

Last Review Date: 08.21

Line of Business: Commercial, Medicaid

[Revision Log](#)

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

### Description

Osilodrostat (Isturisa<sup>®</sup>) is a cortisol synthesis inhibitor.

### FDA Approved Indication(s)

Isturisa is a cortisol synthesis inhibitor indicated for the treatment of adult patients with Cushing's disease (CD) 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<sup>™</sup> that Isturisa is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Cushing's Disease (must meet all):

1. Diagnosis of CD;
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 has not been curative;
  - b. Member is not eligible for pituitary surgery;
5. Dose does not exceed 30 mg twice daily.

**Approval duration: 6 months**

##### B. 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. 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 30 mg twice daily.

**Approval duration: 12 months**

##### B. 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*

CD: Cushing's disease  
FDA: Food and Drug Administration  
UFC: urinary free cortisol

*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 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.
- Across sampled U.S. laboratories (Mayo Clinic Laboratories, LabCorp, Quest Diagnostics), 24-hour UFC adult reference values range from 3 to 64 mcg/24 h. The American Association of Neurological Surgeons notes that UFC levels higher than 50-100 mcg/24 h in adults suggest the presence of Cushing's syndrome [inclusive of CD]. In this context, the Endocrine Society notes that 24-hour UFC levels may range from more than 5 times normal in severe cases to as low as 1.5 times normal in relatively mild cases.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
CD	<p><u>Recommended Dosage, Titration, and Monitoring</u></p> <ul style="list-style-type: none"> <li>• Initiate dosing at 2 mg orally twice daily, with or without food.</li> <li>• Initially, titrate the dosage by 1 to 2 mg twice daily, no more frequently than every 2 weeks based on the rate of cortisol changes, individual tolerability and improvement in signs and symptoms of Cushing's disease. If a patient tolerates Isturisa dosage of 10 mg twice daily and continues to have elevated 24-hour urine free cortisol (UFC) levels above upper normal limit, the dosage can be titrated further by 5 mg twice daily every 2 weeks. Monitor cortisol levels from at least two 24-hour urine free cortisol collections every 1-2 weeks until adequate clinical response is maintained.</li> <li>• The maintenance dosage of Isturisa is individualized and determined by titration based on cortisol levels and patient's signs and symptoms.</li> <li>• The maintenance dosage varied between 2 mg and 7 mg twice daily in clinical trials. The maximum recommended maintenance dosage of Isturisa is 30 mg twice daily.</li> <li>• Once the maintenance dosage is achieved, monitor cortisol levels at least every 1-2 months or as indicated.</li> </ul> <p><u>Dosage Interruptions and Modifications</u></p> <ul style="list-style-type: none"> <li>• Decrease or temporarily discontinue Isturisa if urine free cortisol levels fall below the target range, there is a rapid decrease in cortisol</li> </ul>	60 mg/day

Indication	Dosing Regimen	Maximum Dose
	<p>levels, and/or patients report symptoms of hypocortisolism. If necessary, glucocorticoid replacement therapy should be initiated.</p> <ul style="list-style-type: none"> <li>• Stop Isturisa and administer exogenous glucocorticoid replacement therapy if serum or plasma cortisol levels are below target range and patients have symptoms of adrenal insufficiency.</li> <li>• If treatment is interrupted, re-initiate Isturisa at a lower dose when cortisol levels are within target ranges and patient symptoms have been resolved.</li> </ul>	

**VI. Product Availability**

Tablets: 1 mg, 5 mg, 10 mg

**VII. References**

1. Isturisa Prescribing Information. Lebanon, NJ: Recordati Rare Disease, Inc.; March 2020. Available at [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2020/212801s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212801s000lbl.pdf). Accessed April 5, 2021.
2. Nieman LK, Biller BM, Findling JW, et al. Treatment of Cushing's syndrome: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2015; 100: 2807.
3. Cushing's syndrome/disease. American Association of Neurological Surgeons. Available at <https://www.aans.org/en/Patients/Neurosurgical-Conditions-and-Treatments/Cushings-Disease>. Accessed April 5, 2021.
4. Biller BMK, Newell-Price J, Fleseriu M, et al. OR16-2 Osilodrostat treatment in Cushing's disease (CD): Results from a phase III, multicenter, double-blind, randomized withdrawal study (LINC 3). Journal of the Endocrine Society. 2019. 3(Suppl 1): OR16-2, <https://doi.org/10.1210/js.2019-OR16-2>.
5. Fleseriu M, Pivonello R, Young J, et al. Osilodrostat, a potent oral 11b-hydroxylase inhibitor: 22-week, prospective, phase II study in Cushing's disease. Pituitary (2016) 19:138–148. DOI 10.1007/s11102-015-0692-z.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.21.20	08.20
3Q 2021 annual review: no significant changes; references reviewed and updated.	04.05.21	08.21

**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.

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