Pharmacy Policy Bulletin: J-0264 Isturisa (osilodrostat) – Commercial and Healthcare Reform	
Number: J-0264	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.)** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0264-008	**Original Date:** 06/03/2020
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product:	• Isturisa (osilodrostat)
FDA-Approved Indication:	• Treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom pituitary surgery is not an option or has not been curative.

Background:	• 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. • Cushing's syndrome is a rare condition that causes excess cortisol in the body. Cushing's disease is caused by a pituitary gland tumor that over-secretes the adrenocorticotropic hormone (ACTH), leading to overstimulation of the adrenal glands' cortisol production. • Signs and symptoms of Cushing's disease may include weight gain, fatty tissue deposits, hypertension, abnormal glucose tolerance, lethargy, and depression. • The Endocrine Society guidelines for the treatment of Cushing's syndrome recommend complete surgical resection of the primary lesion(s) underlying Cushing's disease, unless surgery is not possible or unlikely to significantly reduce glucocorticoid excess. For patients who underwent a non-curative surgery or for whom surgery was not possible, second-line treatment options include additional surgeries, radiotherapy, and pharmacological therapy. The choice of medication therapy should be guided by efficacy, individual patient factors, and cost. The goal is clinical normalization using reduction of cortisol levels as a proxy endpoint. • Of the pharmacological treatment options, cabergoline and pasireotide are recommended treatment options for patients with Cushing's disease who are not surgical candidates or who have persistent disease following surgery. Levoketoconazole, ketoconazole, metyrapone, mitotane, and etomidate are recommended as second-line treatment options following surgery with or without radiotherapy in patients with Cushing's disease. Mifepristone is recommended in

	patients with diabetes or glucose intolerance who are not surgical candidates or who have persistent disease after surgery. • Urinary free cortisol (UFC) measurements are used primarily in the diagnosis of hypercortisolism caused by Cushing's syndrome. In normal circumstances, less than 5% of circulating cortisol is free (unbound). Free cortisol is the physiologically active form of cortisol and is filterable by renal glomeruli. With increased levels of plasma cortisol, free cortisol levels increase, which is then filtered through the glomeruli. The concentration of plasma free cortisol correlates well with urinary free cortisol. • Prescribing considerations: ○ Isturisa should be prescribed by an endocrinologist. ○ The maintenance dose of Isturisa is individualized and determined by titration based on UFC levels and a patient's signs and symptoms. ○ Hypokalemia and hypomagnesemia should be corrected prior to starting Isturisa. ○ Obtain a baseline electrocardiogram (ECG). Repeat within one week of treatment initiation, and as clinically indicated thereafter. ○ If treatment is interrupted, re-initiate Isturisa at a lower dose when cortisol levels are within target ranges and patient symptoms have been resolved.

Approval Criteria

I. Initial Authorization
When a benefit, coverage of Isturisa may be approved when all of the following criteria are met **(A., B., and C.)**:
A. The member is 18 years of age or older.
B. The member has a documented diagnosis of Cushing's syndrome (ICD-10: E24).
C. The member meets one (1) of the following criteria **(1. or 2.):**
1. The member is not a candidate for pituitary surgery.
2. Pituitary surgery has not been curative.

II. Reauthorization
When a benefit, reauthorization of Isturisa may be approved when all of the following criteria are met **(A. and B.):**
A. The member has experienced a reduction in the 24-hour mean urinary free cortisol (mUFC) levels from baseline.
B. The prescriber attests that the member has experienced an improvement in signs and symptoms of Cushing's syndrome from baseline.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support their effectiveness and safety in other conditions.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Isturisa [package insert]. Lebanon, NJ: Recordati Rare Disease, Inc.; March 2025.
2. Medscape. Urinary Free Cortisol. Available at: https://emedicine.medscape.com/article/2088848-overview#a4. Accessed October 14, 2021.
3. DRUGDEX System (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; 2024.
4. Clinical Pharmacology OnLine, Tampa, FL: Elsevier 2021. Osilodrostat. Accessed October 9, 2023.
5. UpToDate. Medical Therapy of Hypercortisolism (Cushing's syndrome). Available at: https://www.uptodate.com. Accessed March 9, 2020.