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PHARMACY POLICY STATEMENT
HAP CareSource™ Marketplace

DRUG NAME	Isturisa (osilodrostat)
BILLING CODE	Must use valid NDC
BENEFIT TYPE	Pharmacy
SITE OF SERVICE ALLOWED	Home
STATUS	Prior Authorization Required

Isturisa is a cortisol synthesis inhibitor indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative. It inhibits 11beta-hydroxylase (CYP11B1), the enzyme responsible for the final step of cortisol biosynthesis in the adrenal gland.
Cushing's Syndrome is a disorder of excess cortisol which can be of an exogenous cause, for example from taking glucocorticoids, or it can be endogenous. Endogenous Cushing's Syndrome is rare, with the most common type being Cushing's Disease, which is caused by a pituitary adenoma that secretes excess adrenocorticotropic hormone (ACTH), a hormone responsible for cortisol production. Cortisol is a hormone made by the adrenal glands and has a role in many body functions. First-line treatment is surgical resection of the adenoma.

Isturisa (osilodrostat) will be considered for coverage when the following criteria are met:

Cushing's Disease

For **initial** authorization:

1. Member is 18 years old or older; AND
2. Medication must be prescribed by or in consultation with an endocrinologist; AND
3. Member has a diagnosis of Cushing's disease, with an elevated urinary free cortisol (UFC) level (lab report required); AND
4. Member had pituitary surgery and it was not curative OR member is not a candidate for surgery (documentation required); AND
5. Member has tried ketoconazole or metyrapone for at least 3 months with inadequate response.
6. **Dosage allowed/Quantity limit:** Initiate 2 mg orally twice daily; titrate per package insert; max recommended dose is 30mg (as three 10mg tablets), twice daily. (QL: 180 tablets per 30 days).
   Note: The maintenance dosage varied between 2 mg and 7 mg twice daily in clinical trials.

If all the above requirements are met, the medication will be approved for 6 months.

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For **reauthorization**:
1. Labs must show an improved UFC level compared to pre-treatment; AND
2. Chart notes must show the member has improved signs and symptoms of disease (e.g., weight, fasting glucose, blood pressure, or tumor size).

If all the above requirements are met, the medication will be approved for an additional 12 months.

HAP CareSource considers Isturisa (osilodrostat) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
06/30/2020	New policy for Isturisa created.
03/28/2022	Transferred to new template. Added new references. Elaborated on dosing information. Added metyrapone as a trial option. In renewal, changed UFC normal range to improved UFC.

References:

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2. Recordati Rare Diseases: Isturisa(R) (osilodrostat) Phase III LINC-4 Trial Meets Its Primary Endpoint in Cushing's Disease. Barron's. https://www.barrons.com/press-release/recordati-rare-diseases-isturisa-r-osilodrostat-phase-iii-linc-4-trial-meets-its-primary-endpoint-in-cushing-s-disease-01592380982?tesla=y. Published June 17, 2020. Accessed June 30, 2020.
3. Nieman, LK. Medical therapy of hypercortisolism (Cushing's syndrome). *UpToDate*. https://www.uptodate.com. Updated 6/29/20. Accessed 6/30/20.
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6. Fleseriu M, Pivonello R, Young J, et al. Osilodrostat, a potent oral 11β-hydroxylase inhibitor: 22-week, prospective, Phase II study in Cushing's disease. *Pituitary*. 2015;19(2):138-148. doi:10.1007/s11102-015-0692-z
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8. Fleseriu M, Auchus R, Bancos I, et al. Consensus on diagnosis and management of Cushing's disease: a guideline update. *Lancet Diabetes Endocrinol*. 2021;9(12):847-875. doi:10.1016/S2213-8587(21)00235-7
9. Castinetti F, Nieman LK, Reincke M, Newell-Price J. Approach to the Patient Treated with Steroidogenesis Inhibitors. *J Clin Endocrinol Metab*. 2021;106(7):2114-2123. doi:10.1210/clinem/dgab122
10. Castinetti F, Guignat L, Giraud P, et al. Ketoconazole in Cushing's disease: is it worth a try?. *J Clin Endocrinol Metab*. 2014;99(5):1623-1630. doi:10.1210/jc.2013-3628

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