osilodrostat (Isturisa®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO190

Description

Osilodrostat (Isturisa) is an orally administered cortisol synthesis inhibitor. It inhibits 11beta-hydroxylase (CYP11B1), the enzyme responsible for the final step of cortisol biosynthesis in the adrenal gland.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
osilodrostat (Isturisa)	1 mg tablets	Cushing's disease	180 tablets/30 days
	5 mg tablets		
	10 mg tablets		

Initial Evaluation

I. Osilodrostat (Isturisa) may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with endocrinologist; **AND**
   C. Documentation of baseline Urinary Free Cortisol (UFC) level; **AND**
   D. A diagnosis of **Cushing's disease** when the following are met:
      1. Pituitary surgery is not an option **OR** cortisol levels remain abnormal following attempted resection; **AND**
      2. Treatment with TWO of the following has been ineffective, not tolerated, or all are contraindicated:
         i. Ketoconazole; **OR**
         ii. Cabergoline (Dostinex); **OR**
         iii. Metyrapone (Metopirone); **OR**
         iv. Mitotane (Lysodren); **AND**
      3. Treatment with pasireotide (Signifor) has been ineffective, contraindicated, or not tolerated.

II. Osilodrostat (Isturisa) is considered investigational when used for all other conditions.

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms (e.g., cortisol level has decreased from baseline)

Supporting Evidence

I. The safety and efficacy of osilodrostat (Isturisa) has been studied inpatients 18 years of age or older, and there is no published data to support its use in pediatric patients.
II. Cushing's disease is a serious and complex disease state that requires the supervision of a specialist (e.g. endocrinologist).
III. Cushing's disease is a condition of pathological hypercortisolism that includes demonstrable clinical features. The goals of treating are to eliminate its primary cause and achieve remission so as to eliminate the associated signs, symptoms, and comorbidities and to improve quality of life (QOL).
IV. Osilodrostat (Isturisa) is indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.
V. Osilodrostat (Isturisa) was studied in one prospective, multicenter, open-label, phase III trial with a double-blind, placebo-controlled, randomized withdrawal period in 137 patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.
    - The primary efficacy outcome was the proportion of patients maintaining complete response a mean urinary free cortisol (mUFC) ≤ upper limit of normal (ULN) without a dose increase during the randomized withdrawal period at week 34.
    - At the time of the randomization (Week 26) all (100%) randomized patients were biochemically controlled (mUFC ≤ ULN). At the end of the 8-week randomized withdrawal period (Week 34 of study), the complete response rate in the osilodrostat (Isturisa) group dropped to 86.1% but was higher than that in the placebo group (29.4%).

- The key secondary endpoint was the proportion of patients with mUFC≤ULN at week 24 (end of open-label osilodrostat treatment period 2) without dose-up titration weeks 13-24 and 72/137 patients met the endpoint

VI. According to the Endocrine Society Clinical Practice Guideline, first line treatment is transsphenoidal surgery (TSS) regardless of the cause. Although surgical treatment is optimal, medical therapy is often required when surgery is delayed, contraindicated, or unsuccessful. Medical therapy options within guidelines consist of steroidogenesis inhibitors (i.e. ketoconazole, metyrapone, mitotane, etomidate), pituitary-directed (i.e. cabergoline, pasireotide), and glucocorticoid antagonists (i.e. mifepristone). Guidelines do not prefer one medical therapy over another; however, guidelines do recommend glucocorticoid antagonists (i.e. mifepristone) in patients with diabetes or glucose intolerance who are not surgical candidates or who have persistent disease after TSS.
Guidelines have not been updated to include osilodrostat (Isturisa) in the treatment of Cushing's disease.

VII. There is a lack of head-to-head trials and scientific evidence to show superiority of one medication over the other, however more established therapies include steroidogenesis inhibitors (i.e. ketoconazole, metyrapone, mitotane, etomidate), pituitary-directed (i.e. cabergoline, pasireotide) and glucocorticoid antagonists (i.e. mifepristone). The safety and efficacy of osilodrostat (Isturisa) was assessed in a 48-week long study. Long term safety and efficacy has not been established.

Investigational or Not Medically Necessary Uses

I. Osilodrostat (Isturisa) has not been FDA-approved, or sufficiently studied for safety and efficacy for any other conditions or settings except for patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

References

1. Isturisa [Prescribing Information]. Recordati Rare Disease, Inc: Lebanon, NJ USA 08833. March 2020.
2. Lynnette K. Nieman, Beverly M. K. Biller, James W. Findling, et al. Lynnette K. Nieman, Beverly M. K. Biller, James W. Findling, John Newell-Price, Martin O. Savage, Paul M. Stewart, Victor M. Montori, The Diagnosis of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline, The Journal of Clinical Endocrinology & Metabolism, Volume 93, Issue 5, 1 May 2008, Pages 1526–1540, https://doi-org.liboff.ohsu.edu/10.1210/jc.2008-0125
3. American Association of Neurological Surgeons. Cushing's Syndrome/Disease. (n.d.). Retrieved June 29, 2020, from https://www.aans.org/en/Patients/Neurosurgical-Conditions-and-Treatments/Cushings-Disease

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	07/2020