Isturisa

I. Generic Name:
- a. Osilodrostat

II. Brand Name:
- a. Isturisa

III. Medication Class:
- a. Cortisol synthesis inhibitor

IV. FDA Approved Uses:
- a. Cushing disease: Treatment of Cushing disease in adults for whom pituitary surgery is not an option or has not been curative

V. Application of Criteria:
- a. The following criteria apply to Michigan Medicaid, Illinois Medicaid, and Meridian Choice (HIX)

VI. Criteria for Use:
- a. Documentation of an FDA approved indication
- b. Member must be 18 years of age or older
- c. Request submitted by Endocrinology
- d. Documentation of features consistent with Cushing's syndrome (e.g. facial plethora, proximal myopathy, striae, easy bruising)
- e. Exclusion of physiologic hypercortisolism (e.g. pregnancy, severe obesity, psychological stress, poorly controlled diabetes mellitus, chronic alcoholism, obstructive sleep apnea)
- f. Documentation of two different first-line tests consistent with Cushing's syndrome
- g. Current clinical documents with plan of care recommending treatment with Isturisa
- h. Clinical documentation establishing that the member is not a candidate for surgery or that surgery has not been curative
- i. Clinical documentation of adequate trial and failure of ketoconazole
- j. Clinical documentation of adequate trial and failure of ketoconazole in combination with metyrapone

VII. Required Medical Information:
- a. Proper diagnosis and documentation of an FDA approved indication
- b. Current endocrinology progress notes detailing the diagnosis with current plan of care
- c. Complete endocrinology progress notes documenting the disease and treatment history

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d. Documentation of dose, date ranges of therapy, and clinical outcomes for all medications previously tried and failed
e. Related lab work/test results establishing diagnosis (first-line tests: late-night salivary cortisol, 24-hour urinary free cortisol excretion, overnight dexamethasone suppression test)
f. Related lab work/test results documenting response to previous therapies (serum cortisol, 24-hour urine cortisol excretion)
g. Chart notes showing compliance to previous therapy and office visits

VIII. Contraindications:

a. There are no contraindications listed in the manufacturer's labeling

IX. Not Approved If:

a. Patient shows non-compliance with previous treatment
b. Request is for a non-FDA approved indication or dose
c. Member is a candidate for surgery
d. Request to be used in combination with other medications for the treatment of Cushing's syndrome

X. Length of Authorization:

a. Initial: 1 month
b. Continuation: 3 months

XI. Dosing:

a. Initial dosage: 2mg twice daily
b. Dosage titration: Titrate by 1 to 2 mg twice daily no more frequently than every 2 weeks according to rate of cortisol changes, tolerability, and clinical response. If patient tolerates a dosage of 10 mg twice daily but cortisol target is not achieved, dosage may be increased by 5 mg twice daily every 2 weeks
c. Maintenance dosage: 2 to 7 mg twice daily is a usual maintenance dose

XII. Criteria for Continuation of Therapy:

a. Initial therapy was tolerated
b. Patient must be compliant with taking the medication as prescribed
c. Patient must not be experiencing any severe adverse reaction while taking the medication
d. Current office visit notes/clinical update submitted with each request
e. Submission of serum cortisol and 24-hour urine cortisol excretion documenting response to therapy

XIII. Criteria for Discontinuation of Therapy:

a. Patient is non-compliant with pharmacologic/non-pharmacologic therapy
b. No demonstrable clinically significant improvement after initiation and stabilization of drug therapy
c. Patient is non-responsive to FDA-approved dosing

XIV. References:

1. Facts and Comparisons. Wolters Kluwer Health. April 2020.
2. Isturisa (osilodrostat) [prescribing information]. Lebanon, NJ: Recordati Rare Disease Inc: March 2020.
3. Braun LT, Riester A, Oßwald-Kopp A, et al. Toward a diagnostic score in Cushing's syndrome. Front Endocrinol (Lausanne). 2019; 10: 766. doi:10.3389/fendo.2019.00766[PubMed 31787931]
4. Castinetti F, Guignat L, Giraud P, et al. Ketoconazole in Cushing's disease: is it worth a try? J Clin Endocrinol Metab 2014; 99:1623.
5. Daniel E, Aylwin S, Mustafa O, et al. Effectiveness of Metyrapone in Treating Cushing's Syndrome: A Retrospective Multicenter Study in 195 Patients. J Clin Endocrinol Metab 2015; 100:4146.
6. Duggan S. Osilodrostat: First Approval. Drugs 2020; 80:495.
7. McCance DR, Hadden DR, Kennedy L, et al. Clinical experience with ketoconazole as a therapy for patients with Cushing's syndrome. Clin Endocrinol (Oxf) 1987; 27:593.
8. Schteingart DE. Drugs in the medical treatment of Cushing's syndrome. Expert Opin Emerg Drugs 2009; 14:661.
9. Verhelst JA, Trainer PJ, Howlett TA, et al. Short and long-term responses to metyrapone in the medical management of 91 patients with Cushing's syndrome. Clin Endocrinol (Oxf) 1991; 35:169.
10. Young J, Bertherat J, Vantyghem MC, et al. Hepatic safety of ketoconazole in Cushing's syndrome: results of a Compassionate Use Programme in France. Eur J Endocrinol 2018; 178:447.

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Approved by: _____ Date: _____

CMO

Initial Approval:	
Revised:	
Annual Review:	
Next Review Date:	