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Last P&T Approval/Version: 07/30/2025
Next Review Due By: 07/2026
Policy Number: C19328-A

Isturisa (osilodrostat)

PRODUCTS AFFECTED

Isturisa (osilodrostat)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Cushing's syndrome

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. CUSHING'S SYNDROME:
1. Documented diagnosis of endogenous Cushing's syndrome
   AND
2. Documentation that Cushing syndrome specific surgery has not been curative or member is not a

candidate for surgery
AND

3. Prescriber attests that hypokalemia and hypomagnesemia have been corrected and a baseline electrocardiogram has been done prior to starting Isturisa (osilodrostat) therapy per labeled recommendations
AND
4. Documentation of trial (12 weeks) and failure, serious side effects, or contraindication to ketoconazole therapy
AND
5. Documentation of baseline elevated urinary free cortisol

CONTINUATION OF THERAPY:

A. CUSHING'S SYNDROME:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Documentation member has had a decrease in urinary free cortisol from baseline levels
AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity (e.g., hypocortisolism, hypokalemia, worsening of hypertension, edema, hirsutism) See Appendix

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of Cushing's syndrome. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

Maximum recommended dosage is 30 mg twice daily (See Appendix)
Maximum Quantity Limits – Minimum quantity of both strengths necessary to make dose

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:

Cortisol Synthesis Inhibitors

FDA-APPROVED USES:

Indicated for the treatment of endogenous hypercortisolemia in adults with Cushing's syndrome for whom surgery is not an option or has not been curative.

COMPENDIAL APPROVED OFF-LABELED USES:

Drug and Biologic Coverage Criteria
None

APPENDIX

APPENDIX:

Recommended Dosage, Titration, and Monitoring; Dosage Interruptions and Modifications

The maintenance dosage of Isturisa is individualized and determined by titration based on cortisol levels and patient's signs and symptoms. Decrease or temporarily discontinue Isturisa if urine free cortisol levels fall below the target range, there is a rapid decrease in cortisol levels, and/or patients report symptoms of hypocortisolism. If necessary, glucocorticoid replacement therapy should be initiated. 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. If treatment is interrupted, re-initiate Isturisa at a lower dose when cortisol levels are within target ranges and patient symptoms have been resolved.

See full Prescribing Information for recommendations on symptom mitigation, dose reduction, temporary discontinuation, and discontinuation.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Cushing's disease (CD), or pituitary-dependent Cushing's syndrome (CS), is a severe endocrine disease caused by a corticotroph pituitary tumor and associated with increased morbidity and mortality. CD is the most common cause of endogenous CS. The goal of treatment is to rapidly control cortisol excess and achieve long-term remission, to reverse the clinical features and reduce long-term complications associated with increased mortality. (Cuevas-Ramos et al.) Endogenous CS is a serious, debilitating and rare multisystem disorder. It is caused by the overproduction of cortisol (a steroid hormone that increases blood sugar levels) by the adrenal glands. CS occurs in about 20,000 people in the United States, mostly women between the ages of 20 and 50. The treatment of choice in endogenous Cushing syndrome, which is most commonly caused by a corticotroph pituitary adenoma, is surgical removal of the adenoma. Second-line therapies include medical therapy, bilateral adrenalectomy, and radiation therapy. The therapy must be individualized and targeted at normalization of hormone excess, long-term disease control, and reversal of comorbidities caused by the underlying pathology. In patients in whom surgery has failed, medical therapies are considered palliative and are focused on modifying the hypothalamic/pituitary index, activity of the adrenal gland, and activity of the glucocorticoid receptor. Pharmacological agents currently used in the treatment of CD are classified according to their mechanism of action as adrenal steroidogenesis inhibitors, pituitary-directed drugs and glucocorticoid receptor antagonists: (Cuevas-Ramos D et al. 2014)

- Adrenal-blocking (to reduce adrenal steroidogenesis): ketoconazole, metyrapone, mitotane, etomidate
- Pituitary-directed (centrally acting agents that suppress ACTH secretion by the pituitary;

dopamine agonist: cabergoline and the somatostatin analog: pasireotide): cabergoline, pasireotide

- Glucocorticoid receptor-antagonizing drugs (blocks the peripheral effects of glucocorticoids): mifepristone

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Isturisa (osilodrostat) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Isturisa (osilodrostat) include: No labeled contraindications.

Exclusions/Discontinuation:

Decrease or temporarily discontinue ISTURISA if urine free cortisol levels fall below the target range, there is a rapid decrease in cortisol levels, and/or patients report symptoms of hypocortisolism. If necessary, glucocorticoid replacement therapy should be initiated. 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. If treatment is interrupted, re-initiate ISTURISA at a lower dose when cortisol levels are within target ranges and patient symptoms have been resolved.

OTHER SPECIAL CONSIDERATIONS:

None

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:
Isturisa TABS 1MG
Isturisa TABS 5MG
Isturisa TABS 10MG

REFERENCES

1. Isturisa (osilodrostat) tablets, for oral use [prescribing information]. Bridgewater, NJ: Recordati Rare Disease Inc.; April 2025.
2. Biller BMK, Grossman AB, Stewart PM, et al. Treatment of adrenocorticotropin-dependent Cushing's syndrome: A consensus statement. J Clin Endocrinol Metab. 2008;93:2454- 2462.
3. Tritos NA, Biller BM. Advances in medical therapies for Cushing's syndrome. Discov Med. 2012;13(69):171-179.
4. Rizk A, Honegger J, Milian M and Psaras T. Treatment options in Cushing's disease. ClinMed Insights Oncol. 2012(6):75-84.
5. 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.
6. Fleseriu, M., Auchus, R., Bancos, I., Ben-Shlomo, A., Bertherat, J., Biermasz, N. R., … Biller, B.M. (2021). Consensus on diagnosis and management of Cushing's Disease: A Guideline Update. The Lancet Diabetes & Endocrinology, 9(12), 847–875. doi:10.1016/s2213-8587(21)00235-7

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Diagnosis Required Medical Information Duration of Approval FDA-Approved Uses Contraindications/Exclusions/ Discontinuation References	Q3 2025

REVISION- Notable revisions: Required Medical Information Continuation of Therapy Quantity References	Q3 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Appendix References	Q3 2023
REVISION- Notable revisions: Required Medical Information Duration of Approval Prescriber Requirements	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file