

Endogenous Hypercortisolemia in Cushing's Syndrome

RAPIDLY NORMALIZE

CORTISOL

 Isturisa®
(osilodrostat)

Patient portrayals

QUICK START GUIDE

INDICATIONS AND USAGE

ISTURISA® (osilodrostat) is 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.

IMPORTANT SAFETY INFORMATION

Hypocortisolism: ISTURISA lowers cortisol levels and can lead to hypocortisolism and sometimes life-threatening adrenal insufficiency. Lowering of cortisol can cause nausea, vomiting, fatigue, abdominal pain, loss of appetite, and dizziness. Significant lowering of serum cortisol may result in hypotension, abnormal electrolyte levels, and hypoglycemia.

Hypocortisolism can occur at any time during ISTURISA treatment. Evaluate patients for precipitating causes of hypocortisolism (infection, physical stress, etc.). Monitor 24-hr urine free cortisol, serum or plasma cortisol, and patient's signs and symptoms periodically during ISTURISA treatment.

Please see Important Safety Information throughout and accompanying full Prescribing Information.

The starting dose

Start your patient on ISTURISA® (osilodrostat) 2 mg twice daily with or without food¹

Some patient populations may require modifications to their starting dose¹

Recommended starting dose for patients with hepatic impairment¹

- Child-Pugh B: 1 mg twice daily
- Child-Pugh C: 1 mg once daily in the evening
- More frequent monitoring of adrenal function may be required during dose titration in all patients with hepatic impairment

Recommended starting dose for patients with renal impairment¹

- No dose adjustment is required
- Interpret urinary free cortisol (UFC) levels, cautiously, as they may be reduced in patients with moderate to severe renal impairment¹

Modifications to the dose of ISTURISA may be necessary in patients concomitantly treated with strong CYP3A4 inhibitors (eg, itraconazole, clarithromycin) or with strong CYP3A4 and CYP2B6 inducers (eg, carbamazepine, rifampin, phenobarbital).^a Monitor your patients' cortisol levels, and signs and symptoms during concomitant treatment with these medications while taking ISTURISA

CYP3A4 Inhibitors

For patients taking strong CYP3A4 inhibitors, reduce the dose of ISTURISA by half.

CYP3A4 and CYP2B6 Inducers

For patients taking strong CYP3A4 and CYP2B6 inducers, an increase in ISTURISA dosage may be needed based on the patient's signs and symptoms, and cortisol concentration. Upon discontinuation of strong CYP3A4 and CYP2B6 inducers, a reduction in ISTURISA dosage may be necessary based on the patient's signs and symptoms, and cortisol concentration.

Ask your patients about their current medications and history of hepatic or renal impairment.

What to test for prior to starting ISTURISA¹

- ✓ Test potassium and magnesium levels and correct for hypokalemia and hypomagnesemia
- ✓ Obtain baseline electrocardiogram (ECG)

^aPlease see full Prescribing Information for complete dosing recommendations.

Important Safety Information (continued)

Hypocortisolism (continued): 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. 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. After ISTURISA interruption or discontinuation, cortisol suppression may persist beyond the 4-hour half-life of ISTURISA.

Educate patients on the symptoms associated with hypocortisolism and advise them to contact a healthcare provider if they occur.

Titration the dose

Titrate ISTURISA® (osilodrostat) in 1- or 2-mg increments twice daily, no more than once every 2 weeks, based on the rate of cortisol changes, individual tolerability, and improvement in signs and symptoms of Cushing's syndrome¹

- If your patient tolerates 10 mg twice daily and continues to have elevated 24-hour UFC levels above the upper limit of normal (ULN), you may up-titrate by 5 mg twice daily every 2 weeks
- The maintenance dosage of ISTURISA is individualized and determined by titration based on cortisol levels, and patient's signs and symptoms

Multiple dosing options allow you to adjust therapy for each patient's unique needs during titration and maintenance¹



TABLET SIZES

1 mg¹  6.1 mm²

5 mg¹  7.1 mm³

Continue monitoring your patients to optimize cortisol levels and help improve Cushing's syndrome symptoms¹

- ✓ Monitor cortisol levels from at least two 24-hour UFC collections every 1 to 2 weeks until adequate clinical response is maintained
- ✓ Repeat ECG within 1 week after treatment initiation, and as clinically indicated thereafter
- ✓ Monitor potassium and magnesium levels periodically during treatment with ISTURISA

Important Safety Information (continued)

QTc Prolongation: ISTURISA is associated with a dose-dependent QT interval prolongation which may cause cardiac arrhythmias. Perform an ECG to obtain a baseline QTc interval measurement prior to initiating therapy with ISTURISA and monitor for an effect on the QTc interval thereafter.

Correct hypokalemia and/or hypomagnesemia prior to ISTURISA initiation and monitor periodically during treatment with ISTURISA. Use with caution in patients with risk factors for QT prolongation and consider more frequent ECG monitoring.

Please see Important Safety Information throughout and accompanying full Prescribing Information.



Consider up-titrating your patients slowly¹

Dose increases are recommended no more frequently than every 2 weeks, but may be titrated more slowly based on patient tolerability¹



“Reductions in cortisol levels during osilodrostat therapy can lead to hypocortisolism, which may be mitigated by slow dose up-titration.”⁴
–Fleseriu et al, *Endocrine Practice*

Consider down-titration, temporary discontinuation, or glucocorticoid replacement therapy if any of the following occur¹:

- UFC levels fall below the target range
- Cortisol levels rapidly decrease
- Patients report symptoms of hypocortisolism

Counsel your patients to recognize and report any signs and symptoms of hypocortisolism¹

- Nausea
- Vomiting
- Fatigue
- Abdominal pain
- Loss of appetite
- Dizziness
- Low blood pressure
- Syncope

Significant lowering of serum cortisol may result in hypotension, abnormal electrolyte levels, and hypoglycemia.¹



Hypocortisolism can occur during treatment with ISTURISA[®] (osilodrostat). Stop treatment and administer glucocorticoid replacement therapy if patients are experiencing signs and symptoms of adrenal insufficiency and have cortisol levels below the target range.¹

You may restart treatment with ISTURISA if interrupted¹

Re-initiate ISTURISA at a lower dose when cortisol levels reach the target range and patient symptoms have been resolved.¹

Important Safety Information (continued)

Elevations in Adrenal Hormone Precursors and Androgens: ISTURISA blocks cortisol synthesis and may increase circulating levels of cortisol and aldosterone precursors and androgens. This may activate mineralocorticoid receptors and cause hypokalemia, edema and hypertension. Hypokalemia should be corrected prior to initiating ISTURISA. Monitor patients treated with ISTURISA for hypokalemia, worsening of hypertension and edema. Inform patients of the symptoms associated with hyperandrogenism and advise them to contact a healthcare provider if they occur.

Monitoring and dose adjustments, as needed

Help stay in control by monitoring each patient's changes in cortisol

- The maintenance dosage of ISTURISA® (osilodrostat) is individualized and determined by titration based on cortisol levels and each patient's signs and symptoms¹
- Although the maximum maintenance dosage of ISTURISA is 30 mg twice daily, the maintenance dosage in clinical trials varied between 2 mg and 7 mg twice daily¹

Periodically test once maintenance dosage is achieved¹

- ✓ Monitor cortisol levels at least every 1 to 2 months or as indicated
- ✓ Monitor magnesium and potassium levels
- ✓ Repeat ECG as clinically indicated

Regular monitoring allows you to make more informed titration decisions¹

Important Safety Information (continued)

The most common adverse reactions (incidence >20%) are adrenal insufficiency, fatigue, nausea, headache, edema, decreased appetite, arthralgia, myalgia, and diarrhea.

To report SUSPECTED ADVERSE REACTIONS, contact Recordati Rare Diseases Inc. at 1-888-575-8344, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Drug Interactions

- **CYP3A4 Inhibitor:** Reduce the dose of ISTURISA by half with concomitant use of a strong CYP3A4 inhibitor.
- **CYP3A4 and CYP2B6 Inducers:** An increase of ISTURISA dosage may be needed if ISTURISA is used concomitantly with strong CYP3A4 and CYP2B6 inducers. A reduction in ISTURISA dosage may be needed if strong CYP3A4 and CYP2B6 inducers are discontinued while using ISTURISA.

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 **Isturisa**[®]
(osilodrostat)

The R.A.R.E.[®] Patient Support Program is available to all patients prescribed ISTURISA[®] (osilodrostat)

Designed to ensure your patients taking ISTURISA receive dedicated, multipoint services and support every step of the way.



**ACCESS AND
FINANCIAL
ASSISTANCE**



**EDUCATION
AND ADHERENCE**



**DISPENSING
AND DELIVERY**

Your one-stop source for starting a new patient, plus access to a full range of Recordati Rare Diseases tools and resources.

TO GET YOUR PATIENT STARTED:

**STEP 1:
FILL OUT A PATIENT
PRESCRIPTION FORM**

- Visit [RareResources.com](https://www.rareresources.com) or scan here to download Patient Prescription Forms



**STEP 2:
SUBMIT THE FORM**

- **Fax** the fully completed Patient Prescription Form to Anovo Specialty Rx at **1-855-813-2039**
 - NCPDP #: 4445640
- OR**
- **Electronically submit** the form in your EMR system
 - When ordering, choose **Anovo#5**
 - NCPDP #: 4445640



Recordati Rare Diseases offers a

\$20 CO-PAY

for qualified patients with commercial insurance^a

Contact the R.A.R.E. Patient Support Program for assistance Monday–Friday between 8:00 AM and 8:00 PM ET

Phone: **1-888-855-RARE (7273)**

Fax: **1-855-813-2039**

A clinical pharmacist is always available.

EMR, electronic medical record.

^aEligibility requirements, restrictions, and limitations apply.

R.A.R.E.[®] support for you and your patient

The R.A.R.E. Program will work with you and your patient to validate insurance information, and navigate financial and access assistance

- 1 Once the completed referral form is received, the R.A.R.E. support team will:
 - Investigate your patient's insurance benefits
 - Help coordinate co-pay card assistance
 - Help identify other financial assistance opportunities, if necessary
- 2 A member of the R.A.R.E. team will fax your office the appropriate prior authorization form or provide a CoverMyMeds Key once the benefit investigation is complete
 - Please reach out to the R.A.R.E. team (**1-888-855-7273**) if you have questions regarding required documentation or laboratory testing for prior authorization
- 3 Once benefits have been established, a pharmacist will contact your patient to arrange for overnight delivery of ISTURISA[®] (osilodrostat)

These services are provided at no additional cost to your patient by Recordati Rare Diseases. Information provided is for educational purposes only and is not intended to replace the care and advice of patients' health care providers.

After enrollment, our R.A.R.E. outreach team assists your patients proactively, and on demand, throughout their ISTURISA journey



- Regular calls to the patient, which may assist the provider in assessing their adherence and experience
- You will be alerted if any issues arise that require your attention or need patient follow-up
- Pharmacy support is available 24/7

Visit [RareResources.com](https://www.rareresources.com) for your one-stop source to starting a new patient, plus access to a full range of Recordati Rare Diseases tools and resources.

Important Safety Information (continued)

Use in Specific Populations

- **Lactation:** Breastfeeding is not recommended during treatment with ISTURISA and for at least one week after treatment.

Dosage Interruptions and Modifications: If treatment is interrupted, re-initiate ISTURISA at a lower dose when cortisol levels are within target ranges and patient symptoms have been resolved.

ISTURISA[®] (osilodrostat) tablets, for oral use, is available as 1 mg and 5 mg tablets.

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or visit [RareResources.com](https://www.rareresources.com) to download



Scan here to download the
Patient Prescription Form



R.A.R.E.[®]

Recordati **A**ccess, **R**esources, and **E**ngagement

A collaboration of support and services



Fill out and fax the Patient Prescription Form to 1-855-813-2039 or electronically submit in your EMR system.



A representative from R.A.R.E.[®] will investigate patient insurance benefits, discuss the co-pay program and other financial assistance, and support any prior authorization requirements.



Once benefits have been established, a pharmacist will contact your patient to arrange for overnight delivery of ISTURISA.

Contact the R.A.R.E. Patient Support Program for assistance

Monday-Friday between 8:00 AM and 8:00 PM ET

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References: 1. Isturisa. Package insert. Recordati Rare Diseases, Inc; 2025. 2. Data on file 1. Recordati Rare Diseases Inc; 2020. 3. Data on file 2. Recordati Rare Diseases Inc; 2020. 4. Fleseriu M, Auchus RJ, Snyder PJ, et al. Effect of dosing and titration of osilodrostat on efficacy and safety in patients with Cushing's disease (CD): results from two phase III trials (LINC3 and LINC4). *Endocr Pract.* 2021;27(suppl 6):S112. Abstract #999926. doi:10.1016/j.eprac.2021.04.707.

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 **RECORDATI
RARE DISEASES**
Focused on the Few[®]

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