

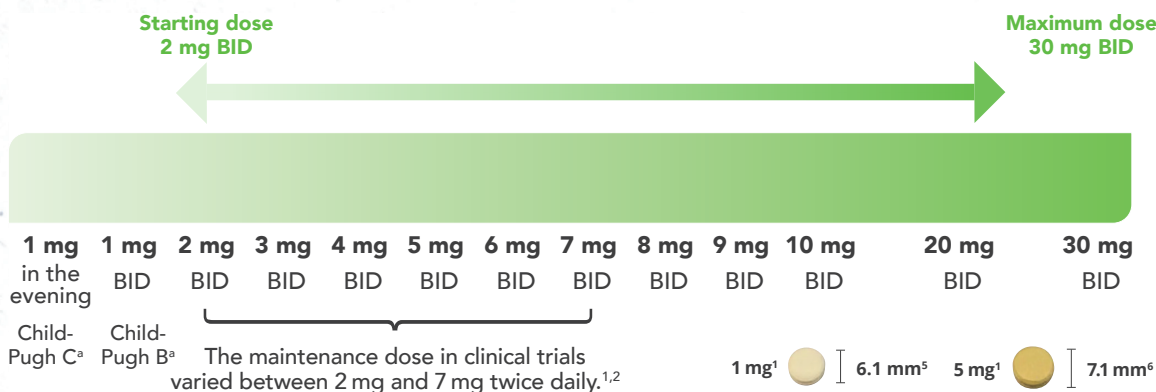


INDICATIONS AND USAGE

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.

YOUR QUICK REFERENCE TO FLEXIBLE DOSING¹

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



The recommended starting dose for patients with moderate hepatic impairment (Child-Pugh B) is 1 mg twice daily; for patients with severe hepatic impairment (Child-Pugh C), the recommended starting dose is 1 mg once daily in the evening.

01 →

START

ISTURISA® (osilodrostat) 2 mg twice daily **with or without food**^{1,a}

02 →

TITRATE

Up 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 syndrome. If your patient tolerates 10 mg twice daily and continues to have elevated 24-hour UFC levels above the ULN, you may up-titrate by 5 mg twice daily every 2 weeks¹

03 →

MONITOR

Cortisol levels every 1 to 2 weeks until adequate clinical response is maintained. Consider less frequent monitoring thereafter. Monitor 24-hour UFC, serum or plasma cortisol, and patient's signs and symptoms periodically during treatment¹



To learn more,
visit [ISTURISA.com/hcp](https://www.isturisa.com/hcp)
or scan here

^aThe recommended starting dose for patients with moderate hepatic impairment (Child-Pugh B) is 1 mg twice daily; for patients with severe hepatic impairment (Child-Pugh C), the recommended starting dose is 1 mg once daily in the evening.¹
BID, twice a day; UFC, urinary free cortisol; ULN, upper limit of normal.

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.

Please see additional Important Safety Information on the back and accompanying full Prescribing Information.

IMPORTANT SAFETY INFORMATION (continued)

Hypocortisolism (continued): 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.

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.

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.

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.

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.

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.

References: 1. Isturisa. Package insert. Recordati Rare Diseases Inc; 2023. 2. 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 3. Fleseriu M, Newell-Price J, Pivonello R, et al. Long-term outcomes of osilodrostat in Cushing's disease: LINC 3 study extension. *Eur J Endocrinol.* 2022;187(4):531-541. doi:10.1530/EJE-22-0317 4. Gadelha M, Bex M, Feelders RA, et al. Randomized trial of osilodrostat for the treatment of Cushing disease. *J Clin Endocrinol Metab.* 2022;107(7):e2882-e2895. doi:10.1210/clinem/dgac178 5. Data on file 1. Recordati Rare Diseases Inc; 2020. 6. Data on file 2. Recordati Rare Diseases Inc; 2020.

Please see additional Important Safety Information on the front and accompanying full Prescribing Information.