Recorlev[1]
Recorlev is a cortisol synthesis inhibitor indicated for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom surgery is not an option or has not been curative. Recorlev has demonstrated in two successful multinational Phase 3 studies to significantly suppress serum cortisol and the on-going open label study will gather further useful information related to the long-term use of Recorlev. When prescribed Recorlev, patients and their healthcare teams have comprehensive, ongoing full-service support from the team at Xeris CareConnection™ to help manage treatment every step of the way.

Cushing's Syndrome[2]
Endogenous CS is a rare, serious endocrine disorder caused by chronic exposure to elevated levels of cortisol; left untreated, it can be fatal. Often the result of a benign tumor of the pituitary gland that tells the body to overproduce high levels of cortisol for a sustained period of time. CS results in physical and emotional signs and symptoms that are debilitating for those living with CS. It is most common among adults aged 30 to 50 years and is more prevalent in females, accounting for 70% of cases.

Cushing's syndrome can cause potential life-threatening complications such as:

- High blood sugar/diabetes
- High blood pressure
- High cholesterol
- Fragile blood vessels, skin, muscle, and bone
- Depression
- Anxiety
- Insomnia

Women with CS may experience additional health issues from CS including:[2-6]

- Menstrual problems
- Hirsutism (coarse body hair growth), acne, and oily skin due to excess male hormones (androgens), primarily testosterone
- Difficulty becoming pregnant

1. Recorlev [package insert]. Chicago, IL: Xeris Pharmaceuticals; 2021
2. The National Institute of Diabetes and Digestive and Kidney Diseases Health Information Center. Cushing's Syndrome. Accessed Sept. 14, 2020. https://www.niddk.nih.gov/health-information/endocrine-diseases/cushings-syndrome.

Indication & Important Safety Information for Recorlev® (levoketoconazole)

BOXED WARNING: HEPATOTOXICITY AND QT PROLONGATION
HEPATOTOXICITY
Cases of hepatotoxicity with fatal outcome or requiring liver transplantation have been reported with oral ketoconazole. Some patients had no obvious risk factors for liver disease. Recorlev is associated with serious hepatotoxicity. Evaluate liver enzymes prior to and during treatment.

QT PROLONGATION
Recorlev is associated with dose-related QT interval prolongation. QT interval prolongation may result in life-threatening ventricular dysrhythmias such as torsades de pointes. Perform ECG and correct hypokalemia and hypomagnesemia prior to and during treatment.

INDICATION

Recorlev is a cortisol synthesis inhibitor indicated for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom surgery is not an option or has not been curative.

Limitations of Use

Recorlev is not approved for the treatment of fungal infections.

CONTRAINDICATIONS

- Cirrhosis, acute liver disease or poorly controlled chronic liver disease, baseline AST or ALT> 3 times the upper limit of normal, recurrent symptomatic cholelithiasis, a prior history of drug induced liver injury due to ketoconazole or any azole antifungal therapy that required discontinuation of treatment, or extensive metastatic liver disease.
- Taking drugs that cause QT prolongation associated with ventricular arrythmias, including torsades de pointes.
- Prolonged QTcF interval > 470 msec at baseline, history of torsades de pointes, ventricular tachycardia, ventricular fibrillation, or prolonged QT syndrome.
- Known hypersensitivity to levoketoconazole, ketoconazole or any excipient in Recorlev.
- Taking certain drugs that are sensitive substrates of CYP3A4 or CYP3A4 and P-gp.

WARNINGS AND PRECAUTIONS

Hepatotoxicity

Serious hepatotoxicity has been reported in patients receiving Recorlev, irrespective of the dosages used or the treatment duration. Drug-induced liver injury (peak ALT or AST greater than 3 times upper limit of normal) occurred in patients using Recorlev. Avoid concomitant use of Recorlev with hepatotoxic drugs. Advise patient to avoid excessive alcohol consumption while on treatment with Recorlev. Routinely monitor liver enzymes and bilirubin during treatment.

QT Prolongation

1. Recorlev [package insert]. Chicago, IL: Xeris Pharmaceuticals; 2021
2. The National Institute of Diabetes and Digestive and Kidney Diseases Health Information Center. Cushing's Syndrome. Accessed Sept. 14, 2020. https://www.niddk.nih.gov/health-information/endocrine-diseases/cushings-syndrome.

Use Recorlev with caution in patients with other risk factors for QT prolongation, such as congestive heart failure, bradyarrythmias, and uncorrected electrolyte abnormalities, with more frequent ECG monitoring considered. Routinely monitor ECG and blood potassium and magnesium levels during treatment.

Hypocortisolism

Recorlev lowers cortisol levels and may lead to hypocortisolism with a potential for life-threatening adrenal insufficiency. Lowering of cortisol levels can cause nausea, vomiting, fatigue, abdominal pain, loss of appetite, and dizziness. Significant lowering of serum cortisol levels may result in adrenal insufficiency that can be manifested by hypotension, abnormal electrolyte levels, and hypoglycemia. Routinely monitor 24-hour urine free cortisol, morning serum or plasma cortisol, and patient's signs and symptoms for hypocortisolism during treatment.

Hypersensitivity Reactions

Hypersensitivity to Recorlev has been reported. Anaphylaxis and other hypersensitivity reactions including urticaria have been reported with oral ketoconazole.

Risks Related to Decreased Testosterone

Recorlev may lower serum testosterone in men and women. Potential clinical manifestations of decreased testosterone concentrations in men may include gynecomastia, impotence and oligospermia. Potential clinical manifestations of decreased testosterone concentrations in women include decreased libido and mood changes.

ADVERSE REACTIONS

Most common adverse reactions (incidence > 20%) are nausea/vomiting, hypokalemia, hemorrhage/contusion, systemic hypertension, headache, hepatic injury, abnormal uterine bleeding, erythema, fatigue, abdominal pain/dyspepsia, arthritis, upper respiratory infection, myalgia, arrhythmia, back pain, insomnia/sleep disturbances, and peripheral edema.

DRUG INTERACTIONS

- Consult approved product labeling for drugs that are substrates of CYP3A4, P-gp, OCT2, and MATE prior to initiating Recorlev.
- Sensitive CYP3A4 or CYP3A4 and P-gp Substrates: Concomitant use of Recorlev with these substrates is contraindicated or not recommended.
- Atorvastatin: Use lowest atorvastatin dose possible and monitor for adverse reactions for dosages exceeding 20 mg daily.
- Metformin: Monitor glycemia, kidney function, and vitamin B12 and adjust metformin dosage as needed.
- Strong CYP3A4 Inhibitors or Inducers: Avoid use of these drugs 2 weeks before and during Recorlev treatment.
- Gastric Acid Modulators: See Full Prescribing Information for recommendations regarding concomitant use with Recorlev.

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2. The National Institute of Diabetes and Digestive and Kidney Diseases Health Information Center. Cushing's Syndrome. Accessed Sept. 14, 2020. https://www.niddk.nih.gov/health-information/endocrine-diseases/cushings-syndrome.

USE IN SPECIFIC POPULATIONS

Lactation: Advise not to breastfeed during treatment and for one day after final dose

To report SUSPECTED ADVERSE REACTIONS, contact Xeris Pharmaceuticals, Inc. at 1-877-937-4737 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Full Prescribing Information including Boxed Warning.

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2. The National Institute of Diabetes and Digestive and Kidney Diseases Health Information Center. Cushing's Syndrome. Accessed Sept. 14, 2020. https://www.niddk.nih.gov/health-information/endocrine-diseases/cushings-syndrome.