

## Recorlev (levoketoconazole)

### Disclaimer

*Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.*

*Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.*

### Summary

Cushing's syndrome (CS), also known as hypercortisolism, refers to a constellation of symptoms that occur from long-term exposure to excess amounts of glucocorticoids (exogenous or endogenous). The exogenous form of Cushing's can result from taking oral corticosteroid medications or external sources. The endogenous form is often caused by tumors within the body that result in the production of excess cortisol or excess adrenocorticotropic hormone (ACTH), which regulates cortisol production. Cortisol, produced in the adrenal glands, helps regulate blood pressure, reduces inflammation, and keeps the heart and blood vessels functioning normally especially in response to stress. The hallmark signs of Cushing syndrome include a fatty hump between the shoulders, a rounded face, and pink or purple stretch marks on the skin. Cushing syndrome can also result in high blood pressure, bone loss and occasionally type 2 diabetes. CS is associated with an increase in morbidity and mortality due to increased risk of events such as blood clots, stroke, and heart attacks.

Treatments for Cushing syndrome can return cortisol levels to normal and improve symptoms. Surgery or radiation are often used as first-line treatments for endogenous CS. Medications can be used to control cortisol production when surgery and radiation are not successful or if a patient is not a candidate for surgical procedures. Medications might also be used before surgery in people who have become very sick with Cushing syndrome to improve signs and symptoms and minimize surgical risk.

Recorlev (levoketoconazole) is FDA approved for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome (CS) for whom surgery is not an option or has not been curative. Recorlev (levoketoconazole) is a cortisol synthesis inhibitor similar to ketoconazole. However, Recorlev (levoketoconazole) is not approved for the treatment of fungal infections. Recorlev's starting dose is 150

mg twice daily taken orally with or without food. The maximum recommended dose is 1,200 mg per day, given as 600 mg twice daily. Since Recorlev (levoketoconazole) can cause numerous adverse effects, patients should be monitored closely while on therapy.

Note: The Plan may require that preferred medications be used first.

### Definitions

“Adrenal glands” are small organs on top of both kidneys that produce hormones regulating a person’s metabolism, immune system, blood pressure, and response to stress.

“Adrenocorticotrophic hormone (ACTH)” is a hormone made in the pituitary gland. Adrenocorticotrophic hormone acts on the outer part of the adrenal gland to control the release of corticosteroid hormones. ACTH is elevated during times of stress.

“Arrhythmia” is a condition in which the heart beats with an irregular or abnormal rhythm.

“Carcinoma” is a cancer arising in the skin tissue or of the lining of internal organs.

“Endogenous” means having an internal cause or origin.

“Exogenous” means having an external cause or origin.

“QT prolongation” occurs when the heart muscle takes a longer time to contract and relax than usual, often causing fast or erratic heartbeats. QT prolongation may increase the risk of developing abnormal heart rhythms and may lead to sudden cardiac arrest.

### Medical Necessity Criteria for Initial Authorization

The Plan considers Recorlev (levoketoconazole) medically necessary when ALL of the following criteria are met:

1. The requested medication is prescribed by, or in consultation with, an endocrine specialist.
2. The member is 18 years of age or older.
3. The member has a confirmed diagnosis of endogenous Cushing’s syndrome.
4. The member does not have a diagnosis of pituitary or adrenal carcinoma.
5. The member is not a candidate for surgery or a previous surgery has not been curative.
6. The member has a documented failure, intolerance, or contraindication to treatment with Signifor (pasireotide).
7. The member does not have a history of liver disease or impairment.
8. The member does not have a history of arrhythmias or QT prolongation.

9. Clinical documentation of a recent baseline 24-hour urinary free cortisol (UFC) is provided as evidence of hypercortisolism (normal cortisol range: 11-138 nmol/day or 4-50 mcg/day).
10. Clinical documentation of a recent baseline liver enzyme function test (LFTs) is provided.
11. Recorlev (levoketoconazole) will not be used concomitantly with any drugs or products that meet BOTH of the following:
  - a. can cause QT prolongation (including but not limited to amiodarone, quinidine, sotalol)
  - b. are involved in the CYP3A4 metabolism cascade (including but not limited to amiodarone, verapamil, diltiazem, proton pump inhibitors (PPIs), statins, other azole type medications or grapefruit juice)
12. Recorlev (levoketoconazole) will be dosed within FDA approved limits or as recommended by case studies or clinical guidelines.
  - a. If dosing outside normal limits, reviewers may consult with Medical Directors or other clinical resources to confirm appropriate dosing.
13. Chart documentation and supporting labwork are provided for review to substantiate the above listed requirements.

If the above prior authorization criteria are met, Recorlev (levoketoconazole) will be approved for 6 months.

#### Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if the member still meets the initial criteria and chart documentation is provided showing the following:

1. The member's condition has improved or stabilized while on Recorlev treatment as evidenced by
  - a. A decrease in 24-hour urinary free cortisol (UFC) from baseline
  - b. Clinical improvement in symptoms based upon prescriber's assessment
2. The member will continue to be monitored for adverse effects including liver function and QT prolongation while on therapy.

Table 1: Dosage and retreatment information

Indication	Initial dose	Maximum dose	Additional Considerations
endogenous hypercortisolemia in adult patients with Cushing's syndrome	150 mg orally twice daily	1,200 mg per day, given as 600 mg orally twice daily	

### Experimental or Investigational / Not Medically Necessary

Recorlev [levoketoconazole] for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

### References

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### Clinical Guideline Revision / History Information

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Reviewed/Revised: