MEDICAL MUTUAL®

Drug Policy

Policy:	Recorlev® (levoketoconazole tablets - Xeris)	Annual Review Date: 03/21/2024 Last Revised Date: 03/21/2024

OVERVIEW

Recorlev, a cortisol synthesis inhibitor, 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. Recorlev was approved through the 505(b)(2) pathway and as such relied upon existing safety and efficacy information for ketoconazole tablets to support approval. Recorlev contains levoketoconazole as the active ingredient. Levoketoconazole is the 2S, 4R-enantiomer derived from racemic ketoconazole.

POLICY STATEMENT

This policy involves the use of Recorlev. Prior authorization is recommended for pharmacy benefit coverage of Recorlev. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Recorlev as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Recorlev be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Recorlev is recommended in those who meet the following criteria:

FDA-Approved Indication:

1. **Endogenous Cushing's Syndrome.**
   Initial Therapy: Approve for 6 months if the patient meets the following criteria (A, B, C, D, E, and F):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Baseline urinary free cortisol is elevated [Documentation Requirements]; AND
   - **C)** According to the prescriber, the patient is not a candidate for surgery or surgery has not been curative; AND
     Note: For a patient with endogenous Cushing's syndrome awaiting surgery or therapeutic response after radiotherapy, see *Other Uses with Supportive Evidence.*
   - **D)** Patient has tried ketoconazole tablets; AND

E) The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of endogenous Cushing's syndrome; AND
F) Baseline laboratory testing, including liver function tests (LFTs), electrocardiogram (ECG), serum potassium, and serum magnesium, have been completed [Documentation Requirements].

Patient is Currently Receiving Recorlev for at least 6 months: Approve for 1 year if the patient meets the following criteria (A, B, C, D, and E):
A) Patient is ≥ 18 years of age; AND
B) According to the prescriber, the patient is not a candidate for surgery or surgery has not been curative; AND
Note: For a patient with endogenous Cushing's syndrome awaiting surgery or therapeutic response after radiotherapy, see *Other Uses with Supportive Evidence.*
C) Patient has tried ketoconazole tablets; AND
D) The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of endogenous Cushing's syndrome; AND
E) The patient has experienced a positive response to therapy, evidenced by a decrease in urinary free cortisol from baseline [Documentation Requirements].

Other Uses with Supportive Evidence

2. **Endogenous Cushing's Syndrome – Patient Awaiting Surgery.** Approve for 4 months if the patient meets the following criteria (A, B, C, D, and E):
A) Patient is ≥ 18 years of age; AND
B) Baseline urinary free cortisol is elevated [Documentation Requirements]; AND
C) Patient has tried ketoconazole tablets; AND
D) The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of endogenous Cushing's syndrome; AND
E) Baseline laboratory testing, including liver function tests (LFTs), electrocardiogram (ECG), serum potassium, and serum magnesium, have been completed [Documentation Requirements].

3. **Endogenous Cushing's Syndrome – Patient Awaiting Therapeutic Response After Radiotherapy.** Approve for 4 months if the patient meets the following criteria (A, B, C, D, and E):
A) Patient is ≥ 18 years of age; AND
B) Baseline urinary free cortisol is elevated [Documentation Requirements]; AND
C) Patient has tried ketoconazole tablets; AND
D) The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of endogenous Cushing's syndrome; AND
E) Baseline laboratory testing, including liver function tests (LFTs), electrocardiogram (ECG), serum potassium, and serum magnesium, have been completed [Documentation Requirements]

Initial Approval/ Extended Approval.
See individual uses for specific approval duration

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Recorlev has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Fungal Infections.** Recorlev is not approved for the treatment of fungal infections.[1]

2. **Concurrent Diagnosis of Pituitary or Adrenal Carcinoma.** Patients with a diagnosis of pituitary or adrenal carcinoma were excluded from Recorlev clinical trials.

3. **Concurrent Diagnosis of Cirrhosis, Extensive Metastatic Liver Disease, Acute Liver Disease, Cholelithiasis, or Liver Disease associated with baseline AST or ALT greater than 3 times the upper limit of normal.** Recorlev is contraindicated in this patient population.[1]

4. **Prior History of Drug Induced Liver Injury due to Ketoconazole or any Azole Antifungal Therapy.** Recorlev is not indicated in those with drug induced liver injury that required discontinuation of therapies mentioned above.[1]

5. **Individual is Currently Using Agents or have Co-morbid Conditions which Prolong the QT Interval.** Recorlev is contraindicated in this patient population [1] (prolonging agents amiodarone, fluoxetine, sertraline, and quetiapine).

6. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Recorlev® tablets [prescribing information]. Chicago, IL: Xeris; June 2023..
2. Sharma ST, Nieman LK, Feelders RA. Cushing's syndrome: epidemiology and developments in disease management. *Clin Epidemiol*. 2015;7:281–293.
3. Tritos NA, Biller BM. Advances in medical therapies for Cushing's syndrome. *Discov Med*. 2012;13(69):171-179.

4. 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.
5. Nieman LK, Biller BM, Findling JW. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2015;100(8):2807-2831.