

PRIOR AUTHORIZATION POLICY

POLICY: Cushing's – Recorlev Prior Authorization Policy

- Recorlev® (levoketoconazole tablets – Xeris)

REVIEW DATE: 01/26/2022

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.

Cushing's syndrome refers to the general state of excessive levels of cortisol (hypercortisolism) in the blood.^{2,3} Hypercortisolism can occur for reasons that are either endogenous or exogenous in nature (e.g., Cushing's disease, cortisol-containing medications, adrenal gland tumor, certain cancers). Cushing's disease (hypercortisolism caused by pituitary adenomas) is the most common type of adrenocorticotrophic hormone (ACTH)-dependent Cushing's syndrome. Treatment for Cushing's syndrome requires a multi-modal approach. The goals of treatment are normalization of cortisol excess, long-term disease control, avoidance of recurrence, and reversal of clinical features.⁴

Guidelines

The Endocrine Society published clinical practice guidelines (2015) for the treatment of Cushing's syndrome.⁵ Recorlev is not addressed in the guidelines. First-line treatment involves resection of the tumor, unless surgery is not possible or is unlikely to meaningfully reduce excess glucocorticoid levels. In patients with ACTH-dependent Cushing's syndrome who underwent non-curative surgery or for whom surgery was not possible, the guidelines advocate several second-line therapies (e.g., repeat transsphenoidal surgery, radiotherapy, medical therapy, and bilateral adrenalectomy). For Cushing's disease, the guidelines recommend all medical therapies as second-line options after transsphenoidal surgery: steroidogenesis inhibitors (ketoconazole, Metopirone® [metyrapone capsules], Lysodren® [mitotane tablets], etomidate) in patients either with or without radiotherapy/radiosurgery; pituitary-directed medical treatments (cabergoline, Signifor® [pasireotide subcutaneous injection]) in patients who are not surgical candidates or who have persistent disease; and Korlym® (mifepristone tablets) in patients with diabetes or glucose intolerance who are not surgical candidates or who have persistent disease after transsphenoidal surgery.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Recorlev. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. 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, approval requires Recorlev to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

1. **Endogenous Cushing's Syndrome.** 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) Patient has hypercortisolemia; 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.

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, and D):
 - A) Patient is ≥ 18 years of age; AND
 - B) Patient has hypercortisolemia; 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.
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, and D):
 - A) Patient is ≥ 18 years of age; AND
 - B) Patient has hypercortisolemia; 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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Recorlev is not recommended in the following situations:

1. **Fungal Infections.** Recorlev is not approved for the treatment of fungal infections.¹
 2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.
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REFERENCES

1. Recorlev® tablets [prescribing information]. Chicago, IL: Xeris; January 2022.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	01/26/2022