



## PRIOR AUTHORIZATION POLICY

**POLICY:** Cushing's – Recorlev Prior Authorization Policy

- Recorlev® (levoketoconazole tablets – Xeris)

**REVIEW DATE:** 01/17/2024

### **INSTRUCTIONS FOR USE**

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

### **CIGNA NATIONAL FORMULARY COVERAGE:**

#### **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.<sup>2,3</sup> 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.<sup>4</sup>

#### **Guidelines**

The Endocrine Society published clinical practice guidelines (2015) for the treatment of Cushing's syndrome.<sup>5</sup> 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<sup>®</sup> [metyrapone capsules], Lysodren<sup>®</sup> [mitotane tablets], etomidate) in patients either with or without radiotherapy/radiosurgery; pituitary-directed medical treatments (cabergoline, Signifor<sup>®</sup> [pasireotide subcutaneous injection]) in patients who are not surgical candidates or who have persistent disease; and Korlym<sup>®</sup> (mifepristone tablets) in patients with diabetes or glucose intolerance who are not surgical candidates or who have persistent disease after transsphenoidal surgery.

A 2021 guideline update does recognize Recorlev as an investigational drug for the treatment of Cushing's syndrome, but do not give recommendations for therapy placement within existing medications.<sup>6</sup>

## **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.

**• Recorlev<sup>®</sup> (levoketoconazole tablets ( Xeris))**  
**is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

### **FDA-Approved Indication**

**1. Endogenous Cushing's Syndrome.** Approve for 1 year if the patient meets the following (A, B, C, D, and E):

**A)** Patient is  $\geq$  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 (A, B, C, and D):

- A) Patient is  $\geq$  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 (A, B, C, and D):

- A) Patient is  $\geq$  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 COVERED**

• **Recorlev® (levoketoconazole tablets ( Xeris)) is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):**

**1. Fungal Infections.** Recorlev is not approved for the treatment of fungal infections.<sup>1</sup>

### **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.
6. Fleseriu M, Auchus R, Bancos I, et al. Consensus on diagnosis and management of Cushing's disease: a guideline update. *Lancet Diabetes Endocrinol.* 2021 Dec;9(12):847-875.

### **HISTORY**

<b>Type of Revision</b>	<b>Summary of Changes</b>	<b>Review Date</b>
Annual Revision	No criteria changes.	01/18/2023
Annual Revision	No criteria changes.	01/17/2024

"Cigna Companies" refers to operating subsidiaries of The Cigna Group. All products and services are provided exclusively by or through such operating subsidiaries, including Cigna Health and Life Insurance Company, Connecticut General Life Insurance Company, Evernorth Behavioral Health, Inc., Cigna Health Management, Inc., and HMO or service company subsidiaries of The Cigna Group. © 2024 The Cigna Group.