Clinical Policy: Levoketoconazole (Recorlev)

Reference Number: PA.CP.PMN.275
Effective Date: 05/2022
Last Review Date: 04/2023

Coding Implications
Revision Log

Description
Levoketoconazle (Recorlev®) is a cortisol synthesis inhibitor.

FDA Approved Indication(s)
Recorlev is indicated for cortisol synthesis inhibitor indicated 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.

Limitation(s) of use: Recorlev is not approved for the treatment of fungal infections.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health and Wellness ® that Recorlev is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cushing's Syndrome (must meet all)**:**

1. Diagnosis of CS;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Surgery has not been curative;
   b. Member is not eligible for surgery;
5. Failure of ketoconazole, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 1,200 mg per day.

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Therapy

A. Cushing's Syndrome (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (*see Appendix D*);
3. If request is for a dose increase, new dose does not exceed 1,200 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CS: Cushing's syndrome
FDA: Food and Drug Administration
UFC: urinary free cortisol

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ketoconazole	400 to 1,600 mg PO daily, administered BID or TID	1,600 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s):
  - Cirrhosis, acute liver disease or poorly controlled liver disease
  - Baseline aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 30 times the upper limit of normal
  - Recurrent symptomatic cholelithiasis
  - Prior history of drug induced liver injury due to ketoconazole or any azole antifungal therapy
  - Taking drugs that cause QT prolongation associated with ventricular arrhythmias
- Boxed warning(s): hepatotoxicity, QT prolongation

Appendix D: General Information
- Positive treatment response for CS includes, but is not limited to, normalization of cortisol levels or action at its receptors to eliminate signs and symptoms of the disease. A 24-hour urinary free cortisol (UFC) level may be used to assess normalization of cortisol levels. The American Association of Neurological Surgeons notes that UFC levels higher than 50-100 mcg/24 h in adults suggest the presence of CS. Dexamethasone suppression test or late night salivary cortisol concentrations may also be used to assess normalization of cortisol levels.
- The use of ketoconazole for the treatment of CS is considered off-label. However, ketoconazole is known to block multiple adrenal enzymes which is its understood mechanism in the treatment of CS. Ketoconazole is recommended as a second-line treatment by the 2015 Endocrine Society Clinical Practice Guidelines with moderate

quality of evidence as a steroidogenesis inhibitor,and is also endorsed by the 2021 Pituitary Society Guideline Update.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CS	Starting dose is 150 mg PO BID. May increase by 150 mg daily, no more frequently than 2-3 weeks based on 24-hour urine free cortisol levels and patient tolerability	1,200 mg/day, administered as 600 mg BID

V. Product Availability

Tablet: 150 mg

VI. References

1. Recorlev Prescribing Information. Chicago, IL: Xerix Pharmaceuticals, Inc.; December 2021. Available at: www.recorlev.com/full-prescribing-information.pdf. Accessed January 4, 2023.
2. Nieman LK, Biller BM, Findling JW, et al. Treatment of Cushing's syndrome: An Endocrine Society Clinical practice guideline. J Clin Endocrinol Metab. 2015;100(8):2807-2831.
3. Fleseriu M, Auchus R, Bancos I, et al. Consensus on diagnosis and management of Cushing's disease: a guideline update. Lancet Diabetes Endocrinol. 2021;9(12):847-875.
4. Cushing's syndrome/disease. American Association of Neurological Surgeons. Available at https://www.aans.org/en/Patients/Neurosurgical-Conditions-and-Treatments/Cushings-Disease. Accessed January 23, 2023.
5. Pivonello R, Elenkova A, Fleseriu M, et al. Levoketoconazole in the treatment of patients with Cushing's syndrome and diabetes mellitus: Results from the SONICS phase 3 study. Front Endocrinol (Lausanne). 2021;12:595894. Published 2021 Apr 7.
6. ClinicalTrials.gov. Study to assess the safety and efficacy of levoketoconazole in the treatment of endogenous Cushing's syndrome. Available at: https://clinicaltrials.gov/ct2/show/NCT03277690. Accessed January 23, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04/2022	
2Q 2023 annual review: no significant changes; references reviewed and updated.	04/2023	