Clinical Policy Title:	levoketoconazole
Policy Number:	RxA.750
Drug(s) Applied:	Recorlev®
Original Policy Date:	04/18/2022
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Recorlev® is a cortisol synthesis inhibitor indicated for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom surgery is not an option or has not been curative.

Limitations of Use: Recorlev® is not approved for the treatment of fungal infections.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
levoketoconazole (Recorlev®)	Endogenous hypercortisolemia in adult patients with Cushing's syndrome	150 mg orally twice daily initially. Titrate by 150 mg/day no more frequently than every 2 to 3 weeks	1,200 mg/day

Dosage Forms

- Tablets: 150 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Endogenous with Cushing's syndrome (must meet all):

1. Diagnosis of endogenous Cushing's syndrome;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 18 years;
4. Member is not a candidate for surgery, or previous surgery has not been curative;
5. Member does not have a diagnosis of pituitary or adrenal carcinoma;
6. Member must meet the following (a & b):
   a. Documentation of baseline urinary free cortisol;
   b. Documentation of baseline liver enzyme function tests;

7. Failure of ketoconazole at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
8. Maximum dose does not exceed 1,200 mg/day orally.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy (e.g. decrease in urinary free cortisol from baseline);
3. If request is for a dose increase, new dose does not exceed 1,200 mg/day orally.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
AST: aspartate aminotransferase
ALT: alanine transaminase
FDA: Food and drug Administration

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
mifepristone (Korlym®)	Initially 300 mg orally once daily. Increase dose in 300 mg increments, based on clinical response and tolerability.	1,200 mg/day orally but should not exceed 20 mg/kg/day orally
Isturisa	2 mg orally twice daily	60 mg/day orally
Signifor	0.6 mg to 0.9 mg subcutaneously twice daily	1.8 mg/day subcutaneously
Signifor LAR	10 mg intramuscularly once every 4 weeks (every 28 days) initially.	40 mg intramuscularly every 4 weeks intramuscularly
cabergoline*	0.5 to 7 mg/week orally	7 mg/week orally
ketoconazole*	400 mg to 1,600 mg/day orally, divided into 2 to 3 doses	Varies
metyrapone*	500 mg to 6 grams/day orally, divided into 3 to 4 doses	6 g/day
mitotane*	0.5 to 5 grams/day orally, given in 3 divided doses	Max. dosage is dependent on mitotane serum concentrations

Off Label*

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

APPENDIX C: Contraindications*/Boxed Warnings

- Contraindication(s):
  - Cirrhosis, acute liver disease or poorly controlled chronic liver disease, baseline AST or ALT > 3 times the upper limit of normal, recurrent symptomatic cholelithiasis, a prior history of drug induced liver injury due to ketoconazole or any azole antifungal therapy that required discontinuation of treatment, or extensive metastatic liver disease.
  - Taking drugs that cause QT prolongation associated with ventricular arrhythmias, including torsades de pointes.
  - Prolonged QTcF interval > 470 msec at baseline, history of torsades de pointes, ventricular tachycardia, ventricular fibrillation, or prolonged QT syndrome.
  - Hypersensitivity to levoketoconazole, ketoconazole or any excipient in Recorlev®.
  - Taking certain drugs that are sensitive substrates of CYP3A4 or CYP3A4 and P-gp.

  *Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed Warning(s):
  - Hepatotoxicity and QT Prolongation.

APPENDIX D: General Information

- Hypocortisolism: Hypocortisolism has been reported with Recorlev®. Monitor patients for hypocortisolism. Dosage reduction or interruption may be necessary.
- Hypersensitivity Reactions: Hypersensitivity to Recorlev® has been reported. Anaphylaxis has been reported with oral ketoconazole.
- Risks Related to Decreased Testosterone: Recorlev® may lower serum testosterone in men and women. Inform patients to report associated symptoms.

References

1. Recorlev® Prescribing Information. Chicago, IL: Xeris Pharmaceuticals Inc.; May 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=d4c5fead-bc4a-fb02-e053-2a95a90ae4fc&type=display . Accessed March 08, 2022.
2. IPD Analytics Rx Insights_New Drug Review_ Recorlev®_01.2022. Available at: https://secure.ipdanalytics.com/User/Pharma/RxStrategy/Search?q=Recorlev . Accessed March 08, 2022.
3. Clinical Pharmacology [database online] powered by Clinical Key. Tampa, FL: Elsevier, 2022. Accessed with subscription at: https://www.clinicalkey.com/pharmacology/login. Accessed March 08, 2022.
4. Recorlev®, Lexi-Drug. Lexicomp. Wolters Kluwer. Hudson, OH. Available at: http://online.lexi.com. Accessed March 08, 2022.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	03/08/2022	04/18/2022