Clinical Policy Title:	mifepristone
Policy Number:	RxA.194
Drug(s) Applied:	Korlym®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Mifepristone (Korlym®) is a cortisol receptor blocker. It is indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery.

Limitation(s) of use: Do not use for the treatment of type 2 diabetes mellitus unrelated to endogenous Cushing's syndrome.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
mifepristone (Korlym®)	Cushing's syndrome	Starting dose is 300 mg PO once daily. May increase in 300 mg increments to a maximum of 1200 mg once daily. Do not exceed 20 mg/kg per day (dose increase once every 2 to 4 weeks).	1200 mg/day not exceeding 20 mg/kg per day. Renal impairment: Dose not to exceed 600 mg once daily. Mild-to-moderate hepatic impairment: Dose not to exceed 600 mg once daily. Concomitant administration with strong CYP3A inhibitors: Dose not to exceed 900 mg once daily.

Dosage Forms

- Tablets: 300 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 prescriber samples does not guarantee coverage under the provisions 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. Cushing's Syndrome (must meet all):

1. Diagnosis of the following (a and b):
   a. Uncontrolled hyperglycemia secondary to endogenous Cushing's syndrome;
   b. Type 2 diabetes mellitus, impaired glucose tolerance or pre-diabetes as evidenced by a fasting blood glucose, oral glucose tolerance test, or hemoglobin A1C;
2. Prescribed by or in consultation with an endocrinologist;
3. Age is 18 years or older;
4. Surgery to treat Cushing's syndrome was insufficient or member is not a candidate for surgery;
5. At the time of request, member does not have any of the following contraindications:
   a. Concurrent use of simvastatin, lovastatin, or CYP3A substrates with narrow therapeutic ranges (e.g., cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, tacrolimus);
   b. Concurrent long-term corticosteroid use;
   c. If the request is for a female, the member is not pregnant, does not have a history of unexplained vaginal bleeding or endometrial hyperplasia or endometrial carcinoma.
6. Dose does not exceed 1200 mg per day (4 tablets per day) and not exceeding 20 mg/kg/day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met all initial approval criteria listed in this policy;
2. Member is responding positively to therapy (e.g., improved fasting blood glucose, oral glucose tolerance test, or hemoglobin A1C since initiation of therapy);
3. If request is for a dose increase, new dose does not exceed 1200 mg per day (4 tablets per day) and not exceeding 20 mg/kg/day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CPY3A: Cytochrome P450, family 3, subfamily A

APPENDIX B: Therapeutic Alternatives

- Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Pregnancy
  - Patients taking drugs metabolized by CPY3A such as simvastatin or lovastatin, and CYP3A substrates with narrow therapeutic ranges.
  - Patients receiving systemic corticosteroids for lifesaving purposes.
  - Women with a history of unexplained vaginal bleeding or endometrial hyperplasia with atypia or

endometrial carcinoma.
  - Hypersensitivity to mifepristone or to any of the product components.
- Boxed Warning(s):
  - Termination of Pregnancy – Mifepristone has potent antiprogestational effects and will result in the termination of pregnancy. Pregnancy must therefore be excluded before the initiation of treatment with Korlym®, or if treatment is interrupted for more than 14 days in females of reproductive potential.

APPENDIX D: General Information

- Being an antagonist of the progesterone receptor, mifepristone promotes unopposed endometrial proliferation that may result in endometrium thickening, cystic dilatation of endometrial glands, and vaginal bleeding. Korlym® should be used with caution in women who have hemorrhagic disorders or are receiving concurrent anticoagulant therapy. Women who experience vaginal bleeding during Korlym® treatment should be referred to a gynecologist for further evaluation.

References

1. Korlym® Prescribing Information. Menlo Park, CA: Corcept Therapeutics, Inc.; November 2019. Available at www.korlym.com. Accessed February 22, 2021.
2. Nieman LK, Biller BMK, Findling JW et al. Treatment of Cushing's syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2015; 100(8): 2807-2831. February 22, 2021.
3. Standards of medical care in diabetes – 2013: position statement. American Diabetes Association. Diabetes Care 2013; 36(Suppl 1): S11-S66. February 22, 2021.
4. Fleseriu M, Molitch ME, Gross C, et al. A new therapeutic approach in the medical treatment of Cushing's syndrome: glucorticoid receptor blockade with mifepristone. Endocr Pract. March/April 2013; 19(2): 313-326. February 22, 2021.
5. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed February 22, 2021.
6. Mifepristone, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed February 22, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	03/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Drug(s) Applied was updated. 3. Line of Business Policy Applies to was update to all lines of business. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Initial Approval criteria: Commercial and Medicaid approval duration were	07/21/2020	09/14/2020

updated from length of benefit to 6 months. 6. Continued Approval criteria: Commercial and Medicaid approval duration. were updated from length of benefit to 12 months. 7. Dosing information was updated. 8. APPENDIX C was updated to include detailed Boxed warning of Termination of Pregnancy and Contraindication verbiage updated to: - Patients taking drugs metabolized by CPY3A such as simvastatin or lovastatin, and CYP3A substrates with narrow therapeutic range. 9. Patients receiving systemic corticosteroids for lifesaving purpose. 10. References were updated. 11. Dosing Regimen updated to include maximum dose: 1200 mg/day not exceeding 20 mg/kg per day. Renal impairment: do not exceed 600 mg once daily. Mild-to-moderate hepatic impairment: do not exceed 600 mg once daily. Concomitant administration with strong CYP3A inhibitors: do not exceed 900 mg once daily. 12. Initial Approval Criteria and Continued Therapy Approval updated to include “not exceeding 20 mg/kg/day”		
Policy was reviewed: 1. Clinical policy verbiage has been updated as ‘The provision of prescriber samples…’ 2. Initial Approval Criteria:	02/22/2021	06/10/2021

1.A.5.c. was added. 3. APPENDIX A: Abbreviation /Acronym Key was updated. 4. Appendix D: General Information was added. 5. References were updated.		