Clinical Policy: Mifepristone (Korlym)

Reference Number: CP.PHAR.101
Effective Date: 05.01.12
Last Review Date: 02.20 Revision Log
Line of Business: Commercial, HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Mifepristone (Korlym®) is a cortisol receptor blocker.

FDA Approved Indication(s)

Korlym 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.

Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® that Korlym is **medically necessary** when the following criteria are met:

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 ≥ 18 years;
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 and b):
   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;
6. Dose does not exceed 1,200 mg (4 tablets) per day.

Approval duration:
Medicaid/HIM - 6 months

Commercial – Length of benefit

B. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Cushing's Syndrome (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
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 1,200 mg (4 tablets) per day.

Approval duration:
Medicaid/HIM - 12 months
Commercial – Length of benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s):
  - Pregnancy

- Use of simvastatin or lovastatin and CYP3A substrates with narrow therapeutic range
- Concurrent long-term corticosteroid use
- Women with history of unexplained vaginal bleeding
- Women with endometrial hyperplasia with atypia or endometrial carcinoma

- Boxed warning(s): termination of pregnancy

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Cushing's syndrome	Starting dose is 300 mg PO QD. May increase in 300 mg increments (dose increase once every 2 to 4 weeks).	1200 mg/day

VI. Product Availability

Tablets: 300 mg

VII. References

1. Korlym Prescribing Information. Menlo Park, CA: Corcept Therapeutics, Inc.; May 2017. Available at www.korlym.com. Accessed November 5, 2015.
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.
3. 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.
4. American Diabetes Association. Standards of medical care in diabetes—2019. Diabetes Care. 2019; 42(suppl 1): S1-S193. Updated July 31, 2019. Accessed November 5, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added Appendix D: Special Populations Safety Background updates Figure 1: removed gender question to simplify line of questioning to reduce duplication of questions and prospective pregnancy testing question; added hepatic impairment question and exceeded dose question	04.01.15	05.01.15
Policy converted to new template. Age requirement added per PI; specialist requirement retained per 2015 Endocrine Society guideline recommendations; max dosing added per PI; dose adjustments removed; contraindications edited per PI; continuing therapy approval duration reduced to 6 months. Initial therapy: • Edited requirement that members be on anti-diabetic therapy prior to initiation of Korlym to a requirement that includes lifestyle modification but not necessarily anti-diabetic medication. • Edited requirement that uncontrolled glucose intolerance/type 2 diabetes prior to starting Korlym be evidenced by HbA1c to a	03.01.16	04.01.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
requirement that it be evidenced by fasting plasma glucose, an oral glucose tolerance test, or HbA1c per the ADA 2013 guidelines. • Added definition of hypokalemia to hypokalemia contraindication. Continuing therapy: Removed the 25% reduction requirement by an oral glucose tolerance test and replaced it with the requirement that there is an improvement in glycemic control evidenced by fasting plasma glucose, an oral glucose tolerance test, or HbA1c.		
Removed age restriction. Removed lifestyle modification requirement. Duration of approval on re-auth changed from 6 months to 12 months.	03.01.17	04.17
1Q18 annual review: - Policies combined for Medicaid and Commercial lines of business. - Age added. "Adherence to an anti-diabetic regimen" is removed due to verification challenge. - The following contraindications are removed due to verification challenge: history of unexplained vaginal bleeding; endometrial hyperplasia with atypia or endometrial carcinoma. -"Dose does not exceed 1200 mg/day or 20 mg/kg per day, whichever is less" is edited to "Dose does not exceed 1200 mg/day". - - References reviewed and updated.	11.28.17	02.18
1Q 2019 annual review: pregnancy removed as a contraindication; no significant changes; references reviewed and updated.	11.13.18	02.19
1Q 2020 annual review: no significant changes; references reviewed and updated; added HIM line of business.	11.05.19	02.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.