Clinical Policy: Mifepristone (Korlym, Mifeprex)

Reference Number: NH.PHAR.101
Effective Date: 04.25
Last Review Date: 03.25
Line of Business: Medicaid

Revision Log

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

Description

Mifepristone (Korlym®) is a cortisol receptor blocker.

Mifepristone (Mifeprex®) is a progestin antagonist.

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.

Mifeprex is indicated for the medical termination of intrauterine pregnancy through 70 days gestation in combination with misoprostol.

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 mifepristone, Mifeprex, and Korlym are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cushing's Syndrome (Korlym and mifepristone) (must meet all):

1. Diagnosis of uncontrolled hyperglycemia secondary to endogenous Cushing's syndrome;
2. Member has type 2 diabetes mellitus, impaired glucose tolerance or pre-diabetes as evidenced by a fasting blood glucose, oral glucose tolerance test, or hemoglobin A1c;
3. Prescribed by or in consultation with an endocrinologist;
4. Age ≥ 18 years;
5. Surgery to treat Cushing's syndrome was insufficient or member is not a candidate for surgery;
6. If request is for brand Korlym, member must use generic mifepristone* 300 mg tablet, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for generic mifepristone*

7. At the time of request, member does not have any of the following contraindications (a and b):
   a. Concurrent use of drugs metabolized by CYP3A (e.g., 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;
8. Dose does not exceed both of the following (a and b):
   a. 1,200 mg per day;
   b. 4 tablets per day.

Approval duration: 6 months

B. Termination of Intrauterine Pregnancy (Mifeprex and mifepristone) (must meet all)*:

***Hyde Amendment Requirements for Federal Financial Participation**

1. Patient has experienced a miscarriage or early pregnancy loss within the first 70 days of gestation; **OR**
2. Patient is pregnant and within first 70 days of gestation; **AND** (**must meet a or b**):
   a. The pregnancy is the result of an act of rape or incest, and evidence of the act of rape or incest is provided through signed documentation from a law enforcement agency of the united states, any state or local jurisdiction, or from an agency of the United States or of a State or local government that provides health or medical services or a rural health clinic whose principal function is not the performance of abortions; (**Must meet all i through v**):
      i. That the person to whom the drug has been prescribed was reported to have been the victim of an incident of rape or incest;
      ii. The date on which the incident occurred;
      iii. The date on which the report was made, which must have been within 60 days of the date on which the incident occurred;
      iv. The name and address of the victim and the name and address of the person making the report (if different from the victim); and
      v. That the report included the signature of the person who reported the incident;
   b. The woman suffers from a physical disorder, physical injury, or physical illness, including a life-endangering physical condition, that would, as certified by a licensed physician, place the woman in danger of death unless an abortion is performed. AND (must meet i and ii):
      i. Is signed by a licensed physician;
      ii. Contains the name and address of the patient.
   c. Dose does not exceed 200mg on Day 1, followed by 24-48 hours after dosing of 800mcg buccal misoprostol.

Approval duration: One treatment pack (3-day treatment)

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the PDL, the no coverage criteria policy CP.PMN.255; or
   b. For drugs NOT on the PDL, the non-formulary policy CP.PMN.16; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy CP.PMN.53.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in <u>any</u> of the following parameters: improved fasting blood glucose, oral glucose tolerance test, or hemoglobin A1c since initiation of therapy;
3. Member must use generic mifepristone* 300 mg tablet, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for generic mifepristone*
4. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 1,200 mg per day;
   b. 4 tablets per day.

Approval duration: 12 months

B. Termination of Pregnancy (Mifeprex and mifepristone):

1. Must meet initial criteria for continued approval to obtain again.

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the PDL, the no coverage criteria policy CP.PMN.255; or
   b. For drugs NOT on the PDL, the non-formulary policy CP.PMN.16; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy CP.PMN.53.

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.PMN.53 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) Korlym:
  - Pregnancy;
  - Concurrent use of drugs metabolized by CYP3A (e.g., simvastatin, lovastatin), or CYP3A substrates with narrow therapeutic ranges (e.g., cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, tacrolimus);
  - Concurrent systemic corticosteroids for lifesaving purposes (e.g., immunosuppression after organ transplantation);
  - Women with history of unexplained vaginal bleeding or endometrial hyperplasia with atypia or endometrial carcinoma;
  - Known hypersensitivity to mifepristone;
- Boxed warning(s): termination of pregnancy
- Contraindication Mifeprex:
  - Confirmed/suspected ectopic pregnancy or undiagnosed adnexal mass
  - Chronic adrenal failure
  - Concurrent long-term corticosteroid therapy
  - History of allergy to mifepristone, misoprostol, or other prostaglandins
  - Hemorrhagic disorders or concurrent anticoagulant therapy
  - Inherited porphyria
  - Intrauterine device (IUD) in place
- Boxed warning(s): Serious and sometimes fatal infections or bleeding

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).	1,200 mg/day
Termination of Intrauterine Pregnancy	Starting dose is 200mg of Mifeprex on Day 1, followed 24-48 hours after Mifeprex dosing by 800mcg buccal misoprostol	200mg/day

VI. Product Availability

Tablet: 300 mg, 200mg

VII. References

1. Korlym Prescribing Information. Menlo Park, CA: Corcept Therapeutics, Inc.; November 2019. Available at www.korlym.com. Accessed October 18, 2024.

2. Mifeprex Prescribing Information. March 2016. Available at www.accessdata.fda.gov/drugsatfda_docs/label/2016/020687s020lbl.pdf. Accessed March 5, 2025.
3. 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.
4. 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. doi: 10.1016/S2213-8587(21)00235-7.
5. 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.
6. American Diabetes Association. Standards of medical care in diabetes—2023. *Diabetes Care*. 2023; 46(suppl 1): S1-S280. Updated January 1, 2023. Accessed October 27, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	03.25	03.25

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.