

# Drug Policy

<b>Policy:</b>	<b>Korlym (mifepristone 300 mg tablets – Corcept, generic)</b>	<b>Annual Review Date:</b> <b>04/18/2024</b>  <b>Last Revised Date:</b> <b>04/18/2024</b>
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**OVERVIEW**

Korlym, a cortisol receptor blocker, is indicated to control hyperglycemia secondary to hypercortisolism in adults with **endogenous Cushing’s syndrome** who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery.<sup>1</sup>

Korlym should not be used for the treatment of type 2 diabetes mellitus unrelated to endogenous Cushing’s syndrome.<sup>1</sup>

**NOTE:** Korlym carries a Black Box Warning for antiprogestinal effects that will result in termination of pregnancy and requires that pregnancy be excluded on initiation and if therapy is interrupted for 14 or more days.

**POLICY STATEMENT**

This policy involves the use of Korlym. Prior authorization is recommended for pharmacy benefit coverage of Korlym. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Korlym as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Korlym be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

**RECOMMENDED AUTHORIZATION CRITERIA**

Coverage of Korlym is recommended in those who meet the following criteria:

**Food and Drug Administration (FDA) Approved Indications**

**1. Endogenous Cushing’s Syndrome.**

*Initial Therapy:* Approve for 6 months if the patient meets the following criteria (a, b, c, d, e, f, and g):

- a. Patient is ≥ 18 years of age; AND

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- b. Baseline urinary free cortisol is elevated [Documentation Requirements]; AND
- c. Korlym is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of Cushing's syndrome; AND
- d. Korlym is being used to control hyperglycemia secondary to hypercortisolism in patients who have type 2 diabetes mellitus or glucose intolerance AND
- e. According to the prescriber, the patient is not a candidate for surgery or surgery has not been curative; AND  
Note: For a patient with endogenous Cushing's syndrome awaiting surgery or therapeutic response after radiotherapy, see *Other Uses with Supportive Evidence*.
- f. The patient has tried ketoconazole tablets, Metopirone (metyrapone capsules), Lysodren (mitotane tablets), or Signifor/Signifor LAR for the treatment of Cushing's syndrome.
- g. If brand Korlym is prescribed, the patient must meet the following criteria (a and b):
  - a. The patient has previously failed or is intolerant to generic mifepristone; AND
  - b. Brand Korlym is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction [Documentation Required].

Patient is Currently Receiving Korlym for at least 6 months: Approve for 1 year if the patient meets the following criteria (a, b, c, d, e, f, and g):

- a. Patient is  $\geq 18$  years of age; AND
- b. Korlym is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of Cushing's syndrome; AND
- c. Korlym is being used to control hyperglycemia secondary to hypercortisolism in patients who have type 2 diabetes mellitus or glucose intolerance AND
- d. According to the prescriber, the patient is not a candidate for surgery or surgery has not been curative; AND  
Note: For a patient with endogenous Cushing's syndrome awaiting surgery or therapeutic response after radiotherapy, see *Other Uses with Supportive Evidence*.
- e. The patient has tried ketoconazole tablets, Metopirone (metyrapone capsules), Lysodren (mitotane tablets), or Signifor/Signifor LAR for the treatment of Cushing's syndrome; AND
- f. The patient has experienced improved glucose tolerance or stable glucose tolerance while on Korlym [Documentation Requirements].
- g. If brand Korlym is prescribed, the patient must meet the following criteria (a and b):
  - a. The patient has previously failed or is intolerant to generic mifepristone; AND
  - b. Brand Korlym is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction [Documentation Required].

## Initial Approval/ Extended Approval.

A) Initial Approval: 6 months

B) Extended Approval: 1 year

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## Other Uses with Supportive Evidence

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- 2. Endogenous Cushing's Syndrome – Patient Awaiting Surgery.** Approve for 4 months if the patient meets the following criteria (a, b, c, d, e, and f):
- Patient is  $\geq 18$  years of age; AND
  - Baseline urinary free cortisol is elevated [Documentation Requirements]; AND
  - Korylm is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of endogenous Cushing's syndrome.
  - Korlym is being used to control hyperglycemia secondary to hypercortisolism in patients who have type 2 diabetes mellitus or glucose intolerance AND
  - The patient has tried ketoconazole tablets, Metopirone (metyrapone capsules), Lysodren (mitotane tablets), or Signifor/Signifor LAR for the treatment of Cushing's syndrome.
  - If brand Korlym is prescribed, the patient must meet the following criteria (a and b):
    - The patient has previously failed or is intolerant to generic mifepristone; AND
    - Brand Korlym is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction [Documentation Required].
- 3. Endogenous Cushing's Syndrome – Patient Awaiting Response after Radiotherapy.** Approve for 4 months if the patient meets the following criteria (a, b, c, d, e, and f):
- Patient is  $\geq 18$  years of age; AND
  - Baseline urinary free cortisol is elevated [Documentation Requirements]; AND
  - Korylm is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of endogenous Cushing's syndrome.
  - Korlym is being used to control hyperglycemia secondary to hypercortisolism in patients who have type 2 diabetes mellitus or glucose intolerance AND
  - The patient has tried ketoconazole tablets, Metopirone (metyrapone capsules), Lysodren (mitotane tablets), or Signifor/Signifor LAR for the treatment of Cushing's syndrome.
  - If brand Korlym is prescribed, the patient must meet the following criteria (a and b):
    - The patient has previously failed or is intolerant to generic mifepristone; AND
    - Brand Korlym is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction [Documentation Required].

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## CONDITIONS NOT RECOMMENDED FOR APPROVAL

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Korlym has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Exogenous (Iatrogenic) Cushing's Syndrome.** Korlym is not indicated in exogenous Cushing's syndrome. Exogenous Cushing's syndrome is caused by excessive glucocorticoid administration. Therefore, the process to reverse the excessive cortisol exposure is to taper or discontinue the offending drug when possible.
2. **Type 2 Diabetes Not Associated with Endogenous Cushing's Syndrome.** Korlym should not be used for the treatment of type 2 diabetes unrelated to endogenous Cushing's syndrome.
3. **Psychotic Features of Psychotic Depression.** The manufacturer is conducting Phase III studies with mifepristone to treat the psychotic features of psychotic depression. Mifepristone is being investigated as an alternative to electroconvulsive therapy (ECT) or combination drug therapy to determine whether patients with psychotic features of psychotic depression who are treated with mifepristone can be more easily maintained on antidepressant therapy alone without the need for ECT or antipsychotic medication. Individual trials have demonstrated variable efficacy results. In some of the studies comparing mifepristone with placebo, various statistically significant improvements in psychiatric symptoms have been noted with mifepristone relative to placebo; however, the methodology and statistical analyses of some studies have been questioned. Data are inconclusive.
4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

## Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

## REFERENCES

1. Korlym® tablets [prescribing information]. Menlo Park, CA: Corcept Pharmaceuticals; May 2017.
2. Mifeprex® tablets [prescribing information]. New York, NY: Danco Laboratories, LLC; March 2016.
3. Belanoff JK, Rothschild AJ, Cassidy F, et al. An open-label trial of C-1073 (mifepristone) for psychotic major depression. *Biol Psychiatry*. 2002;52:386-392.

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4. Fleseriu M, Biller BMK, Findling JW, et al. Mifepristone, a glucocorticoids receptor antagonist, produces clinical and metabolic benefits in patients with Cushing's syndrome. *J Clin Endocrin Metab.* 2012; 97(6):2039-2049.
5. Biller BMK, Grossman AB, Stewart PM, et al. Treatment of adrenocorticotropin-dependent Cushing's syndrome: A consensus statement. *J Clin Endocrinol Metab.* 2008;93:2454-2462.
6. Tritos NA, Biller BM. Advances in medical therapies for Cushing's syndrome. *Discov Med.* 2012;13(69):171-179.
7. Rizk A, Honegger J, Milian M and Psaras T. Treatment options in Cushing's disease. *Clin Med Insights Oncol.* 2012(6):75-84. 8. Mazziotti G, Gazzaruso C and Giustina A. Diabetes in Cushing syndrome: basic and clinical aspects. *Trends Endocrinol Metab.* 2011;22(12):499-506.