PRIOR AUTHORIZATION POLICY

POLICY: Cushing's – Mifepristone Prior Authorization Policy
- Korlym® (mifepristone 300 mg tablets – Corcept, generic)

REVIEW DATE: 04/19/2024

OVERVIEW

Mifepristone, 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.[1]

Mifepristone should not be used for the treatment of type 2 diabetes mellitus unrelated to endogenous Cushing's syndrome.[1]

Disease Overview

Cushing's syndrome refers to the general state of excessive levels of cortisol (hypercortisolism) in the blood.[2,3] Hypercortisolism can occur for reasons that are either endogenous or exogenous in nature (e.g., Cushing's disease, cortisol-containing medications, adrenal gland tumor, certain cancers). Cushing's disease (hypercortisolism caused by pituitary adenomas) is the most common type of adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome. Treatment for Cushing's syndrome requires a multi-modal approach. The goals of treatment are normalization of cortisol excess, long-term disease control, avoidance of recurrence, and reversal of clinical features.[4]

Guidelines

The Endocrine Society published clinical practice guidelines (2015) for the treatment of Cushing's syndrome.[5] First-line treatment involves resection of the tumor, unless surgery is not possible or is unlikely to meaningfully reduce excess glucocorticoid levels. In patients with ACTH-dependent Cushing's syndrome who underwent non-curative surgery or for whom surgery was not possible, the guidelines advocate several second-line therapies (e.g., repeat transsphenoidal surgery, radiotherapy, medical therapy, and bilateral adrenalectomy). For Cushing's disease, the guidelines recommend all medical therapies as second-line options after transsphenoidal surgery: steroidogenesis inhibitors (ketoconazole tablets, Metopirone® [metyrapone capsules], Lysodren® [mitotane tablets], etomidate injection) in patients either with or without radiotherapy/radiosurgery; pituitary-directed medical treatments (cabergoline tablets, Signifor® [pasireotide subcutaneous injection]) in patients who are not surgical candidates or who have persistent disease; and mifepristone tablets (Korlym®, generic) in patients with diabetes or glucose intolerance who are not surgical candidates or who have persistent disease after transsphenoidal surgery.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of mifepristone. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with mifepristone as well as the monitoring required for adverse events and long-term efficacy, approval requires mifepristone to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

1. **Endogenous Cushing's Syndrome.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Mifepristone is being used to control hyperglycemia secondary to hypercortisolism in patients who have type 2 diabetes mellitus or glucose intolerance; AND
   - **C)** Patient meets ONE of the following (i, ii, or iii):
     - **i.** According to the prescriber, the patient is not a candidate for surgery or surgery has not been curative; OR
     - **ii.** Patient is awaiting surgery for **endogenous Cushing's Syndrome**; OR
     - **iii.** Patient is awaiting therapeutic response after radiotherapy for **endogenous Cushing's Syndrome**; AND
   - **D)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has tried one of ketoconazole tablets, Metopirone (metyrapone capsules), Lysodren (mitotane tablets), Signifor (pasireotide subcutaneous injection), or Signifor LAR (pasireotide intramuscular injection) for the treatment of endogenous Cushing's syndrome; OR
     - **ii.** Patient is currently receiving mifepristone; AND
   - **E)** The medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of Cushing's syndrome.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of mifepristone is not recommended in the following situations:

1. **Type 2 Diabetes Not Associated with Endogenous Cushing's Syndrome.** Mifepristone should not be used for the treatment of type 2 diabetes unrelated to endogenous Cushing's syndrome.[1]

2. **Psychotic Features of Psychotic Depression.** Mifepristone has been used to treat the psychotic features of psychotic depression. Individual trials have demonstrated variable efficacy results.[6,7] 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.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Korlym® tablets [prescribing information]. Menlo Park, CA: Corcept; March 2020.
2. Sharma ST, Nieman LK, Feelders RA. Cushing's syndrome: epidemiology and developments in disease management. *Clin Epidemiol*. 2015;7:281–293.
3. Tritos NA, Biller BM. Advances in medical therapies for Cushing's syndrome. *Discov Med*. 2012;13(69):171-179.
4. 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.
5. Nieman LK, Biller BM, Findling JW. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2015;100(8):2807-2831.
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7. Flores BH, Kenna H, Keller J, et al. Clinical and biological effects of mifepristone treatment for psychotic depression. *Neuropychopharmacology*. 2006;31:628-636