mifepristone (Korlym®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO095

Description

Mifepristone (Korlym) is a cortisol receptor blocker indicated for hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
mifepristone (Korlym)	300 mg tablets	Hyperglycemia secondary to hypercortisolism in Cushing's syndrome	120 tablets/30 days

Initial Evaluation

I. Mifepristone (Korlym) may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an endocrinologist; **AND**
   C. A diagnosis of **hyperglycemia secondary to hypercortisolism in members with endogenous Cushing's syndrome** when the following are met:
      1. Member has a diagnosis of type 2 diabetes **OR** glucose intolerance; **AND**
      2. Baseline hemoglobin A1c (HbA1c) has been provided in this request; **AND**
      3. Member has had an inadequate response to pituitary surgery or is not a candidate for surgery; **AND**
      4. Treatment with TWO of the following has been ineffective, not tolerated, or all are contraindicated:
         i. Ketoconazole; **OR**
         ii. Cabergoline (Dostinex); **OR**
         iii. Metyrapone (Metopirone); **OR**
         iv. Mitotane (Lysodren)

II. Mifepristone (Korlym) is considered not medically necessary when criteria above are not met and/or when used for:
   A. Hypertension associated with Cushing's syndrome
   B. Termination of pregnancy

C. Induction of labor

III. Mifepristone (Korlym) is considered investigational when used for all other conditions, including but not limited to:
   A. Exogenous (Iatrogenic) Cushing's syndrome
   B. Type 2 diabetes related hyperglycemia

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has a reduction in HbA1c from baseline; **AND**
IV. Member has exhibited improvement in Cushing's syndrome manifestation (e.g., cushingoid appearance, acne, hirsutism, striae, psychiatric symptoms, and excess total body weight)

Supporting Evidence

I. The safety and efficacy of mifepristone (Korlym) for the treatment of endogenous Cushing's syndrome was studied in an uncontrolled, open-label, 24-week, multicenter clinical study that enrolled 50 participants. Those participants exhibited clinical and biochemical evidence of hypercortisolemia despite first-line intervention via surgical treatment and radiotherapy. Per label, the reasons for medical treatment was failed surgery, recurrence of disease, and a poor medical candidate for surgery. The study was split into two cohorts, diabetes and hypertension.
   A. The primary efficacy analysis for the diabetes cohort was an analysis of responders (patient who had a ≥25% reduction from baseline in glucose AUC). The primary efficacy analysis was conducted in the modified intent-to-treat population (n=25); 15 of 25 patients (60%) were treatment responders (95% CI: 39%, 78%).
   B. As for the hypertension cohort, there were no changes in mean systolic and diastolic blood pressures at the end of the trial relative to baseline in the modified intent-to-treat population (n=21).
   C. Participants in the study showed varying degrees of improvement in Cushing's syndrome manifestations such as cushingoid appearance, acne, hirsutism, striae, psychiatric symptoms, and excess total body weight.
II. According to the Endocrine Society Clinical Practice Guideline, first line treatment is transsphenoidal surgery (TSS) regardless of the cause. Although surgical treatment is optimal, medical therapy is often required when surgery is delayed, contraindicated, or unsuccessful.

Medical therapy options within guidelines consist of steroidogenesis inhibitors (i.e. ketoconazole, metyrapone, mitotane, etomidate), pituitary-directed treatments (i.e. cabergoline, pasireotide), and glucocorticoid antagonists (i.e. mifepristone). Guidelines do not prefer one medical therapy over another; however, guidelines do recommend glucocorticoid antagonists (i.e. mifepristone) in patients with diabetes or glucose intolerance who are not surgical candidates or who have persistent disease after TSS.

Investigational or Not Medically Necessary Uses

I. Hypertension associated with Cushing's syndrome
   A. In the clinical trial, the hypertension cohort demonstrated no changes in mean systolic and diastolic blood pressures at the end of the trial relative to baseline in the modified intent-to-treat population (n=21).
II. Termination of pregnancy and induction of labor
   A. Although the active ingredient (mifepristone) at a lower strength is indicated for both termination of pregnancy and induction of labor, mifepristone (Korylm) has not been approved by the FDA or studied in those indications.
III. Exogenous (Iatrogenic) Cushing's syndrome
   A. Safety and efficacy has only been established for endogenous Cushing's syndrome, there is currently limited evidence to suggest the use of mifepristone (Korlym) in the setting of exogenous (iatrogenic) Cushing's syndrome.
IV. Type 2 diabetes related hyperglycemia
   A. Safety and efficacy has only been established for hyperglycemia secondary to hypercortisolism in members with endogenous Cushing's syndrome; therefore, hyperglycemia due to type 2 diabetes alone is considered experimental and investigational.

References

1. Korlym [Prescribing Information]. Menlo Park, CA: Corcept Therapeutic, Inc. May 2017.
2. Nieman LK, Biller, BMK, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism*, Volume 100, Issue 8, August 2015, Pages 2807–2831. Available at: https://doi.org/10.1210/jc.2015-1818
3. Scaroni C, Zilio M, Foti M, et al. Glucose Metabolism Abnormalities in Cushing Syndrome: From Molecular Basis to Clinical Management. *Endocrine Reviews,* Volume 38, Issue 3, June 2017, Pages 189–219. https://doi.org/10.1210/er.2016-1105.

Policy Implementation/Update:

Action and Summary of Changes	Date
• Changed criteria regarding previous therapy to require treatment with two agents to have been ineffective, not tolerated, or contraindicated	08/2020

• Updated renewal language to reflect new standard language • Updated supporting evidence	
Transitioned criteria to policy with the following updates: defined surgery in the policy, removed pregnancy question, addition of supporting evidence, and addition of investigational diagnoses along with supporting evidence.	10/2019
Criteria created	09/2012