Korlym (mifepristone)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Korlym (mifepristone) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines, and clinical studies. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Korlym is a cortisol receptor blocker 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.

Limitations of Use

Korlym should not be used for the treatment of patients with type 2 diabetes mellitus unless it is secondary to Cushing's syndrome.

POLICY

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

1. For initial requests:
    - Diagnostic test results confirming diagnosis of Cushing Syndrome including but not limited to:
        - Late-night salivary cortisol (two measurements)
        - Urine free cortisol (UFC; at least two measurements)
        - Overnight 1 mg dexamethasone suppression test (DST)

- Longer low-dose (2 mg/day for 48 hrs) dexamethasone suppression test (DST)
- Documentation supporting inadequate glycemic control and diagnosis of Type 2 diabetes or impaired glucose tolerance/pre-diabetes by fasting plasma glucose, an oral glucose tolerance test, and/or hemoglobin A1c
- Documentation supporting one of the following
  - Surgery to remove the causative tumor did not result in normalization of circulating cortisol levels and associated glucose intolerance
  - Surgical removal is contraindicated, or member is not a candidate for surgery

2. For continuation of therapy:
   - Documentation supporting the clinical benefit of Korlym therapy (i.e., current and baseline hemoglobin A1C level, current and baseline blood glucose levels)

Criteria for Initial Approval

A. Korlym (mifepristone) may be considered **medically necessary** for treatment of hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing syndrome when all of the following criteria are met:
   1. Member has type 2 diabetes mellitus or glucose intolerance
   2. A confirmed diagnosis of hyperglycemia secondary to hypercortisolism in an individual with endogenous Cushing's syndrome.
   3. Member has failed to achieve adequate glycemic control despite individualized diabetic management
   4. Member has had surgery that was not curative OR member is not a candidate for surgery
   5. If the member is able to become pregnant, a negative pregnancy test is required before initiating therapy
   6. Prescribed by, or in consultation with, a board-certified endocrinologist.
   7. Member has failed at least ONE or has a contraindication or medically justifiable reason that precludes the use of ALL the following oral drug therapies:
      - ketoconazole
      - cabergoline
      - metyrapone
      - mitotane

   Approval will be for **6 months**

Continuation of Therapy

A. Korlym (mifepristone) may be considered **medically necessary** for the continued treatment of hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing syndrome when all of the following criteria are met:
   1. The member has experienced a positive clinical benefit to therapy defined as achieving and maintaining improved glycemic control as evidenced by a documented decrease in hemoglobin A1C levels and blood glucose levels
   2. The member continues to be seen by an endocrinologist or is in consultation with an endocrinologist

   Approval will be for **12 months**

Other

Korlym is considered **not medically necessary** for members who do not meet the criteria set forth above.

Members currently receiving the requested medication as samples or via the manufacturer's patient assistance program will be required to meet the criteria for initial approval. This ensures that members are treated equally regardless of their provider's ability to access medication samples.

Dosage and Administration
Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits

- Korlym 300 mg tablets - 4 tablets per day

CLINICAL RATIONALE

Cushing's syndrome is an endocrine disease caused by excessive secretion of adrenocorticotropin hormone (ACTH), which results in excess cortisol secretion. The cause can be due to corticotropin [ACTH]-producing pituitary tumor [Cushing's disease], ectopic ACTH secretion by a nonpituitary tumor, or cortisol secretion by an adrenal adenoma or carcinoma. The goals of treatment in ACTH dependent Cushing's syndrome include reversal of clinical features, normalization of biochemical changes with minimal morbidity, and long-term control without recurrence.

The 2015 Endocrine Society guidelines for the treatment of Cushing's syndrome recommend complete surgical resection of the primary lesion(s) underlying Cushing's disease, unless surgery is not possible or unlikely to significantly reduce glucocorticoid excess. For patients who underwent a noncurative surgery or for whom surgery was not possible, second-line treatment options include additional surgeries, radiotherapy, and pharmacological therapy. Of the pharmacological treatment options, cabergoline and Signifor (pasireotide) are recommended treatment options for patients with Cushing's disease who are not surgical candidates or who have persistent disease following surgery, while ketoconazole, Metopirone (metyrapone), Lysodren (mitotane), and Amidate (etomidate) are recommended as second-line treatment options following surgery with or without radiotherapy in patients with Cushing's disease. Mifepristone is recommended in patients with diabetes or glucose intolerance who are not surgical candidates or who have persistent disease after surgery.

Adrenal enzyme inhibitors (i.e., ketoconazole and metyrapone) are the most commonly used drugs, but adrenolytic agents (i.e., mitotane), drugs that target a pituitary or ectopic tumor (e.g., pasireotide, cabergoline, chemotherapy or immunotherapy), and glucocorticoid-receptor antagonists (i.e., mifepristone) also have been studied and used. Only pasireotide, osilodrostat, and mifepristone have an FDA approved indication for Cushing's disease or syndrome. Note: Metopiron (metyrapone) is not commercially available in the U.S. and must be obtained from HRA Pharma via special allocation only.

Korlym (mifepristone) is an antiprogestational agent, which, at high doses, competitively binds to the glucocorticoid and progesterone receptors. Korlym (mifepristone) is FDA-approved to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery. Korlym should not be used in the treatment of patients with type 2 diabetes unless it is secondary to Cushing's syndrome.

The efficacy of mifepristone was evaluated in a 24-week, uncontrolled, multicenter, open-label trial of 50 patients with Cushing's syndrome associated with either diabetes (N=29) or hypertension (N=21) hypertension and who failed multimodality therapy. Response was defined as at least a 25% decrease in area under the curve for glucose on a standard oral glucose tolerance test from baseline to 24 weeks. In the hypertension cohort, there were no changes in mean systolic and diastolic blood pressure changes at the end of the study compared with baseline. Sixty percent of patients (N=15/25) met the study's primary endpoint and experienced a significant decrease in the area under the curve (AUC) for glucose on an oral

glucose tolerance test. In addition, the mean reduction of HbA1c over the course of the study was 1.1% ($p<0.001$). Antidiabetic medications were reduced in seven of 15 patients. Of 12 patients taking insulin, five reduced their daily dose by at least half. Antidiabetic medications were reduced in seven of 15 patients. Of 12 patients taking insulin, five reduced their daily dose by at least half. Weight reduction and waist circumference decrease were also observed in study subjects. Overall, 87% ($P < 0.0001$) of patients had a significant improvement in clinical and metabolic status. Insulin resistance, depression, cognition, and quality of life also improved.

Adverse events in the open-label trial were reported in 88% of patients during mifepristone treatment, most commonly nausea (48%), fatigue (48%), headache (44%), decreased blood potassium (34%), arthralgia (30%), vomiting (26%), peripheral edema (26%), HTN (24%), dizziness (22%), decreased appetite (20%), and endometrial thickening (20%). Patients should be monitored for adrenal insufficiency, hypokalemia, prolonged QT interval. Pregnancy must be excluded prior to initiation of therapy with Korlym and a nonhormonal form of contraception must be used during treatment and for 1 month after stopping therapy due to the use of mifepristone resulting in termination of pregnancy.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- N/A

REFERENCES

- Korlym [package insert]. Menlo Park, CA: Corcept Therapeutics Incorporated; November 2019.
- Mifepristone [package insert]. Parsippany, NJ: Teva Pharmaceuticals; February 2022.
- Nieman LK, Biller B, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015;100:2807-2831.
- Fleseriu M, et al; SEISMIC Study Investigators. Mifepristone, a glucocorticoid receptor antagonist, produces clinical and metabolic benefits in patients with Cushing's syndrome. J Clin Endocrinol Metab 2012;97:2039-2049.
- Fleseriu M, Auchus R, Bancos I, et al. Consensus on Diagnosis and Management of Cushing's Disease: A Guideline Update. Lancet Diabetes Endocrinol. 2021;9(12):847-875. doi:10.1016/S2213-8587(21)00235-7
- Nieman LK, Biller B, Findling JW, et al. The diagnosis of Cushing's syndrome: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2008;93(5):1526.
- Biller BM, Grossman AB, Stewart PM, et al. Treatment of adrenocorticotropin-dependent Cushing's syndrome: a consensus statement. J Clin Endocrinol Metab 2008;93:2454-2462.

POLICY HISTORY

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