Drug Coverage Policy

Effective Date.....8/1/2024
Coverage Policy Number.....IP0092
Policy Title.....Mifepristone

Cushing's – Mifepristone

- Korlym® (mifepristone 300 mg tablets – Corcept, generic)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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.[1]

Korlym 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 Korlym® (mifepristone tablets) in patients with diabetes or glucose intolerance who are not surgical candidates or who have persistent disease after transsphenoidal surgery.

Medical Necessity Criteria

Mifepristone is considered medically necessary when the following is met:

FDA-Approved Indication

1. **Endogenous Cushing's Syndrome.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E and F):
   - **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.
   - **F)** Preferred product criteria is met for the product(s) as listed in the below table(s)

Employer Plans:

Product	Criteria
Korlym (mifepristone)	Trial of **mifepristone** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction

Individual and Family Plans:

Product	Criteria
Korlym (mifepristone)	Trial of **mifepristone** (the bioequivalent generic product) [may require prior authorization] AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **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.[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.

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.
6. DeBattista C, Belanoff J, Glass S, et al. Mifepristone versus placebo in the treatment of psychosis in patients with psychotic major depression. *Biol Psychiatry.* 2006;60:1343-1349.

7. Flores BH, Kenna H, Keller J, et al. Clinical and biological effects of mifepristone treatment for psychotic depression. *Neuropychopharmacology*. 2006;31:628-636

Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	**Mifepristone tablets added to the policy**. **Endogenous Cushing's Syndrome:** Added a standard of care prerequisite step. Added a preferred product prerequisite step. **Endogenous Cushing's Syndrome – Patient Awaiting Surgery:** Decreased the initial authorization duration from 6 to 4 months. Added a preferred product prerequisite step. **Endogenous Cushing's Syndrome – Patient Awaiting Response after Radiotherapy:** Decreased the initial authorization duration from 6 to 4 months. Added a preferred product prerequisite step. **Added preferred product criteria.** For Korlym on all Employer and IFP formularies.	07/01/2024
Annual Review	**Endogenous Cushing's Syndrome:** A patient who is awaiting surgery and a patient who is awaiting therapeutic response after radiotherapy were added as options of approval; for these conditions patient who is awaiting surgery and a patient who is awaiting therapeutic response after radiotherapy, a requirement was added that the patient has tried one other medication or the patient is currently receiving mifepristone were added. **Endogenous Cushing's Syndrome – Patient Awaiting Surgery:** This condition was removed from the policy and is now addressed under Endogenous Cushing's Syndrome. **Endogenous Cushing's Syndrome – Patient Awaiting Therapeutic Response After Radiotherapy:** This condition was removed from the policy and is now addressed under Endogenous Cushing's Syndrome.	8/1/2024

The policy effective date is in force until updated or retired.