09-J1000-69

Original Effective Date: 06/15/12

Reviewed: 06/10/20

Revised: 07/15/20

Subject: Mifepristone (Korlym™) Oral

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Cushing's syndrome results from prolonged exposure to excessive concentrations of glucocorticoids; it is associated with significant morbidity and mortality with 75% of individuals with uncontrolled disease also have metabolic syndrome, characterized by glucose intolerance, obesity, hypertension, and dyslipidemia.[1] Individuals with Cushing's syndrome produce excess glucocorticoids in response to overproduction of adrenocorticotropin hormone (ACTH; ACTH-dependent) or due to abnormal adrenocortical tissues (ACTH-independent).[1] The treatment of choice for both ACTH-dependent and ACTH-independent Cushing's syndrome is surgical resection of any offending tumors. However, several secondary pharmacologic treatment plans are available, depending on the etiology of the disease.[1]

Mifepristone (Korlym), a selective and potent antagonist of glucocorticoid receptors, was approved by the Food and Drug Administration (FDA) to control hyperglycemia secondary to endogenous Cushing's syndrome in adults with type 2 diabetes mellitus or glucose intolerance who are not candidates for surgery or have failed surgery.[2,3] The clinical data supporting the FDA approval of mifepristone resulted from an uncontrolled, open-label, multicenter, 24-week, phase three study of 50 patients with endogenous Cushing's syndrome, who were either not eligible for surgery or whose condition had relapsed after surgery. Study participants exhibited either glucose intolerance (29 patients) or hypertension (21 patients).[3] Within the glucose-intolerant group, 60% of patients experienced a greater than 25% reduction from baseline in the oral glucose tolerance test. In this group, the mean hemoglobin A1C (HbA1C) value was reduced from 7.4% to 6.3%. All 14 patients with above-normal HbA1C levels at baseline experienced reductions. Eight of these patients experienced normalization of their HbA1C levels. Antidiabetic medications were reduced in 7 of the 15 patients with type 2 diabetes, and remained constant in the others.[3]

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of mifepristone (Korlym™) **meets the definition of medical necessity** to treat hyperglycemia in members meeting **ALL** of the following criteria:

1. Diagnosis of endogenous Cushing's syndrome
2. Member has Type 2 diabetes mellitus or glucose intolerance secondary to Cushing's syndrome
3. Member has an inadequate response to surgery **OR** is not a candidate for surgery
4. Total daily dose does not exceed 1200 mg

Duration of approval: 6 months

Mifepristone (Korlym™) **meets the definition of medical necessity** when used to treat the following designated Orphan Drug indication (http://www.fda.gov/orpha/desinat/list.htm):

1. Ovarian Cancer

Duration of approval: 1 year

Continuation of mifepristone (Korlym™) **meets the definition of medical necessity** for endogenous Cushing's syndrome when the following criteria are met:

A. The member has been previously approved by Florida Blue or another health plan in the past 2 years, OR the member has previously met all indication-specific criteria for coverage
B. Member has a beneficial response to therapy (improved or stable glucose tolerance)
C. The total daily dose does not exceed 1200 mg

Duration of approval: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA Approved

- 300 mg by mouth once daily with food
- May increase daily dose in 300 mg increments every two to four weeks
- Maximum daily dose of 1200 mg, but should not exceed 20 mg/kg/day.

Dose adjustments:

- Renal impairment: do not exceed 600 mg once daily.
- Mild-to-moderate hepatic impairment: do not exceed 600 mg once daily. Do not use in severe hepatic impairment.
- Concomitant administration with strong CYP3A inhibitors: Do not exceed 900 mg once daily.

Drug Availability

- 300 mg tablet

PRECAUTIONS:

Boxed Warning

Termination of pregnancy – pregnancy must be excluded before initiation of treatment or if treatment is interrupted for more than 14 days in females

Contraindications

- Pregnancy
- Drugs metabolized by CYP3A4 (e.g., simvastatin, lovastatin, cyclosporine)
- Concomitant treatment with systemic corticosteroids for serious medical conditions
- History of unexplained vaginal bleeding
- Endometrial hyperplasia with atypia or endometrial carcinoma
- Hypersensitivity to mifepristone

Precautions/Warnings

- Adrenal insufficiency
- Hypokalemia
- Vaginal bleeding and endometrial changes
- QT interval prolongation – QTc interval prolonged in a dose-related manner
- Exacerbation of conditions treated with corticosteroids
- Use of strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, ritonavir, atazanavir, clarithromycin)
- Increased risk of opportunistic infections (e.g., *Pneumocystis jiroveci*)
- Potential Effects of Hypercortisolemia – caution in heart conditions such as heart failure and coronary vascular disease.

BILLING/CODING INFORMATION:

HCPCS Coding:

J8499	Prescription drug, oral, non-chemotherapeutic, NOS

ICD-10 Diagnosis Codes That Support Medical Necessity:

C56.1 – C56.9	Malignant neoplasm of ovary
E24.0	Pituitary dependent Cushing's disease

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

DEFINITIONS:

Cushing's syndrome: is a hormone disorder caused by high levels of cortisol in the blood. This can be caused by taking glucocorticoid drugs, or by tumors that produce cortisol or adrenocorticotropic hormone (ACTH) or CRH.

RELATED GUIDELINES:

H.P. Acthar® Gel, 09-J1000-15

Mitotane (Lysodren®) Tablets, 09-J1000-60

OTHER:

None applicable.

REFERENCES:

1. Clinical Pharmacology [Internet Database]. Gold Standard, Inc., 2020 [cited 2020 May 31]. Available from: http://www.clinicalpharmacology-ip.com/.
2. Ingenix HCPCS Level II, Expert 2012.
3. Ingenix ICD-9-CM for Physicians-Volumes 1 & 2, Expert 2012.
4. KORLYM (mifepristone) tablet. Menlo Park (CA): Corcept, Inc; November 2019. Package insert
5. Micromedex ® Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 5/31/20.
6. Mifepristone. In McEvoy GK, editor. AHFS drug information 2016 [monograph on the internet]. Bethesda (MD): American Society of Health-System Pharmacists; 2016 [cited 2016 June 16].
7. Smith SM. Chapter 85. Adrenal Gland Disorders. In: Talbert RL, DiPiro JT, Matzke GR, Posey LM, Wells BG, Yee GC, eds. Pharmacotherapy: A Pathophysiologic Approach. 8th ed. New York: McGraw-Hill; 2011. http://www.accesspharmacy.com.lp.hscl.ufl.edu/content.aspx?aID=7992321. Accessed April 15, 2013.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/10/20.

GUIDELINE UPDATE INFORMATION:

06/15/12	New Medical Coverage Guideline.
06/15/13	Review and revision to guideline; consisting of description, position statement, dosage/administration, precautions, program exceptions, references; Review status changed to no longer reviewed.
11/01/15	Revision: ICD-9 Codes deleted.
08/15/16	Review and revision to guideline; including update to position statement, coding and references.
07/15/20	Revision to guideline; including update to position statement and references.