mifepristone (Korlym®)

Policy # 00383
Original Effective Date: 08/21/2013
Current Effective Date: 08/23/2017

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider the use of mifepristone (Korlym®)† for use in patients with endogenous Cushing’s syndrome to be eligible for coverage.

Patient Selection Criteria
Coverage eligibility for mifepristone (Korlym) will be considered when all of the following criteria are met:

- Patient has a diagnosis of hyperglycemia secondary to endogenous Cushing’s Syndrome; and
- Patient is 18 years of age or older; and
- Patient has type 2 diabetes mellitus OR glucose intolerance; and
- Patient has failed surgery OR is not a candidate for surgery.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of mifepristone (Korlym) when patient selection criteria are not met to be investigational.*

Background/Overview
Korlym is a cortisol receptor blocker that is approved 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. Korlym is a selective antagonist of the progesterone receptor at low doses and blocks the glucocorticoid receptor (GR-II) at higher doses. Korlym has high affinity for the GR-II receptor but little affinity for the GR-1 (mineralocorticoid) receptor. Each tablet contains 300mg of active ingredient. The recommended starting dose is 300mg once daily with a meal. Based on clinical response and tolerability, the dose may be increased in 300mg increments to a maximum of 1200mg once daily. There are also dosage adjustments for renal and hepatic impairment.

Endogenous Cushing’s Syndrome
Endogenous Cushing’s syndrome is a rare heterogeneous disorder that leads to cortisol excess. Patients with Cushing’s exhibit a variety of signs and symptoms such as high blood pressure, loss of libido, diabetes, weight gain, acne, moon face, truncal obesity, and slender extremities. Goals of treatment include
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normalizing the cortisol excess, avoiding and reversing the clinical features, and controlling the disease long term. Medications available that have the ability to inhibit adrenocortical steroidogenesis include ketoconazole, metyrapone, mitotane, and etomidate.

**FDA or Other Governmental Regulatory Approval**

U.S. Food and Drug Administration (FDA)

Korlym was approved in February of 2012 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. Korlym carries a boxed warning for termination of pregnancy. Korlym has antiprogestational effects and will result in the termination of pregnancy.

**Rationale/Source**

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Korlym was assessed in an uncontrolled, open label trial in patients with evidence of hypercortisolemia despite poor surgical treatment and radiotherapy. There was a diabetes cohort and a hypertension cohort in this study. Treatment with Korlym was started at 300mg once daily and dosages were increased to maximum doses of 900-1200mg per day based on their weight, clinical tolerance, and clinical response. The primary efficacy endpoint for the diabetes cohort was an analysis of responders. A responder was defined as a patient who had a ≥ 25% reduction in glucose area under the curve (AUC). In this study, 60% of the patients (15 of 25) in the diabetes cohort were treatment responders. The median decrease in glucose AUC was 35%. The baseline HbA1c was 7.43 in the diabetes cohort at baseline and decreased to 6.29 at week 24. Fasting plasma glucose was reduced from 149mg/dL to 104mg/dL. Antidiabetic medications were reduced in 7 of the 15 patients taking antidiabetic medications at baseline.

**References**


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Policy History
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08/01/2013 Medical Policy Committee review
08/21/2013 Medical Policy Implementation Committee approval. New policy.
08/07/2014 Medical Policy Committee review
08/20/2014 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/06/2015 Medical Policy Committee review
08/19/2015 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/04/2016 Medical Policy Committee review
08/17/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/03/2017 Medical Policy Committee review
Next Scheduled Review Date: 08/2018

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:
A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
1. Consultation with the Blue Cross and Blue Shield Association TEC or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

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**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.