Korlym™ (mifepristone) Prior Authorization with Quantity Limit Program Summary

This program applies to Commercial, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the prior authorization (PA) requirement for Korlym™ is to encourage appropriate selection of patients for treatment according to product labeling and/or clinical studies and/or guidelines and according to dosing recommended in product labeling. The program will approve for doses within the set limit that do not exceed 20 mg/kg/day. Doses above the set limit will be approved if the requested quantity is below the FDA limit, cannot be dose optimized, and do not exceed 20 mg/kg/day.

TARGET DRUGS

Korlym™ (mifepristone)

QUANTITY LIMIT TARGET DRUGS- RECOMMENDED LIMITS

Brand (generic)	GPI	Multisource Code	Quantity per Day Limit
Korlym™ (mifepristone) oral tablet			
300 mg tablet	27304050000330	M, N, O, or Y	4 tablets

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Initial and Renewal Evaluation

Korlym (mifepristone) will be approved when the following are met:

1. The patient has a diagnosis of Cushing's syndrome
   AND
2. The patient does not have any FDA labeled contraindication(s) to therapy with the requested agent
   AND
3. ONE of the following:
   a. The patient has type 2 diabetes mellitus
      OR
   b. The patient has glucose intolerance as defined as a 2-hr glucose tolerance test glucose value of 140-199 mg/dL
   AND
4. ONE of the following:
   a. The patient has failed surgical resection
      OR
   b. The patient is not a candidate for surgical resection
   AND
5. ONE of the following:
   a. BOTH of the following:
      i. The quantity requested is less than or equal to the program quantity limit
         AND
      ii. The dose does not exceed 20 mg/kg/day
      OR
   b. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
         AND

ii. The requested quantity (dose) is less than or equal to the FDA labeled dose
AND
iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit
AND
iv. The dose does not exceed 20 mg/kg/day

Length of Approval: 12 months

This pharmacy policy is not an authorization, certification, explanation of benefits or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All pharmacy policies are based on (i) information in FDA approved package inserts (and black box warning, alerts, or other information disseminated by the FDA as applicable); (ii) research of current medical and pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment

FDA Indication[1]**:** 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.

Limitation of Use[1]: Do not use for the treatment of type 2 diabetes mellitus unrelated to endogenous Cushing's syndrome.

Dosing[1]**:**
The recommended starting dose is 300 mg once daily as a single dose. The dose may be increased in 300 mg increments no more frequently than once every 2-4 weeks to a maximum of 1200 mg once daily; however, dosing should not exceed 20 mg/kg/day. Decisions about dose increases should be based on clinical response and tolerability. Mifepristone should be taken with a meal.

Clinical Rationale[2-6]
Cushing's syndrome is an endocrine disease caused by excessive secretion of adrenocorticotropin hormone (ACTH) which results in excess cortisol secretion. The majority (80%) of ACTH-dependent Cushing syndrome is caused by a pituitary tumor. Features of hypercortisolism include weight gain, severe fatigue and muscle weakness, high blood pressure, depression, cognitive impairment, easy bruising, hyperpigmentation, loss of libido, hirsutism, acne, menstrual disorders, and diabetes/glucose intolerance. The American Diabetes Association defines impaired glucose tolerance as blood glucose of 140 md/dL to 199 mg/dL (>7.8 mmol/L to <11.1 mmol/L) after the oral glucose tolerance test (OGTT). The OGTT is a two-hour test that checks your blood glucose levels before and 2 hours after drinking a glucose containing drink. The Endocrine Society Guidelines for Cushing's syndrome states that surgical resection of the causal lesion(s) is generally the first-line approach. The choice of second-line treatments, including medication, bilateral adrenalectomy, and radiation therapy (for corticotrope tumors), must be individualized to each patient. An additional consensus echoes the guidelines and states that the treatment of choice for ACTH-dependent Cushing's syndrome is curative surgery. Second-line treatments include more radical surgery, pituitary radiation, medical therapy, and bilateral adrenalectomy.

Safety[1]
Mifepristone has a boxed warning for pregnancy termination. Pregnancy must be excluded prior to initiation of therapy and if treatment is disrupted for more than 14 days. Other contraindications include patients taking simvastatin, lovastatin, or other CYP3A4 substrates with a narrow therapeutic range (e.g. cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus), concomitant systemic corticosteroid use for serious medical conditions (e.g. immunosuppression after organ transplant), and women at risk for vaginal bleeding or endometrial changes.

References

1. Korlym prescribing information. Corcept Therapeutics. May 2017.
2. Korlym Monograph. Prime Therapeutics. February 2012.
3. Biller BMK et al. Treatment of Adrenocorticotropin-Dependent Cushing's Syndrome: A Consensus Statement. *J Clin Endrocrinol Metab* 2008;93:2454-2462.
4. American Diabetes Association. Diagnosing Diabetes and Learning about Prediabetes. June 9, 2015.
5. Nieman L, Beverly M. K. Biller, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism. July 2015.
6. Nieman L, Biller B, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2015;100: 2807–2831.

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