

Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCEND002.0425	ENDOCRINE & METABOLIC DRUGS KORLYM® (mifepristone 300 mg tablets)
Effective Date: 6/1/2025	Review/Revised Date: 10/12, 04/13, 04/14, 04/15, 02/16, 03/17, 03/18, 07/18, 02/19, 03/20, 02/21, 03/22, 02/23, 03/24, 03/25 (JWL)
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Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:

Providence Health Plan and Providence Health Assurance as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

Commercial
Medicaid

POLICY CRITERIA:

COVERED USES:

All Food and Drug Administration (FDA) approved indications not otherwise excluded from the benefit.

REQUIRED MEDICAL INFORMATION:

1. Documentation that the patient has hyperglycemia secondary to endogenous Cushing’s Syndrome (defined as hypercortisolism that is not a result of chronic administration of high dose glucocorticoids), AND
2. Documentation that the patient has type 2 diabetes mellitus or glucose intolerance, AND
3. Documentation that the patient has failed surgery or is not a candidate for surgery

Reauthorization: Documentation that the patient has improved or stable glucose tolerance

EXCLUSION CRITERIA:

Current pregnancy

AGE RESTRICTIONS: N/A

PRESCRIBER RESTRICTIONS:

Must be prescribed by, or in consultation with, an endocrinologist.

**PHARMACY PRIOR AUTHORIZATION
POLICY AND CRITERIA
ORPTCEND002**

**ENDOCRINE & METABOLIC DRUGS
KORLYM®
(mifepristone 300mg tablets)**

COVERAGE DURATION:

Initial authorization for six months. Reauthorization for 12 months.

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:

Mifepristone (Korlym®) 300 mg tablets are indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing syndrome who have type 2 diabetes mellitus or glucose intolerance and who are not candidates for surgery or have not responded to prior surgery. Mifepristone is not indicated for the treatment of type 2 diabetes mellitus **unrelated** to endogenous Cushing syndrome. Mifepristone is a selective antagonist of the progesterone receptor at low doses and blocks the glucocorticoid receptor at higher doses. It has a high affinity for the glucocorticoid receptor, but little affinity for the mineralocorticoid receptor. Mifepristone and its active metabolites have greater affinity for the glucocorticoid receptor than either dexamethasone or cortisol.

**Mifepristone is also available in a 200 mg strength (Mifeprex) indicated as an abortifacient. Only mifepristone 300 mg will be discussed and all information presented below is for the indication of hyperglycemia secondary to hypercortisolism in adult patients with Cushing's syndrome. All other indications are outside of the scope of this policy except as it relates to the safety concerns for women of child-bearing potential.*

FDA APPROVED INDICATIONS:

Korlym® (mifepristone) 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.

POSITION STATEMENT:

Cushing's syndrome, which results from prolonged exposure to inappropriately high levels of the hormone cortisol, can be caused by taking glucocorticoid drugs or by diseases that result in excess cortisol. The most common non-iatrogenic cause of Cushing's is caused by an adenoma in the pituitary gland, and surgical removal is the preferred treatment. Second-line therapies include radiation and medical therapy. Therapeutic goals include normalization of hormone excess (in particular cortisol levels) and long term disease control. In patients in whom surgery has failed, medical therapies are considered palliative and are focused on modifying the activity of the adrenal gland and the glucocorticoid receptor.

Treatment alternatives include ketoconazole, mitotane, and metyrapone, that are adrenal enzyme inhibitors used to reduce adrenal steroidogenesis. Signifor® (pasireotide) is a somatostatin analog and has shown enhanced activity and sustained cortisol reduction properties. Mifepristone is a glucocorticoid receptor antagonist and is involved with blocking the peripheral effects of glucocorticoids however, the hypothalamic-pituitary-adrenal axis feedback loop results in increased circulating cortisol levels as a result of this receptor blockade, thus it is not able to decrease cortisol levels long term.

In the pivotal study for the approval, there was not a sustained reduction in diastolic pressure and the primary endpoint was AUC_{glucose} with a secondary endpoint of HgA1c. Consequently, at this time it is only approved to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing syndrome who have type 2 diabetes mellitus or glucose intolerance.

Korlym® is available through SPARK (support program for access and reimbursement for Korlym®) who coordinates coverage issues and delivery.

Dose optimization: If the member is titrated to a dose that is divisible by 200 mg, recommend the use of mifepristone 200 mg tablets (Mifeprex®), which come in packages of three tablets. An over-ride would need to be added, as this medication is excluded for use in abortions.

REFERENCE/RESOURCES:

1. Fleseriu M, Biller B, Findling J, et al. Mifepristone, a Glucocorticoid Receptor Antagonist, Produces Clinical and Metabolic Benefits in Patients with Cushing's Syndrome. JCEM jc.2011-3350; doi:10.1210/jc.2011-3350.
2. *Korlym* [package insert]. Menlo Park, CA: Corcept Therapeutics Inc; 9/2024.

3. Rizk A, Honegger J, Milian M, Psaras T. Treatment options in Cushing's disease. *Clin Med Insights Oncol.* 2012;6:75-84
4. Korlym. Formulary Monograph Service. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; June 2012. Accessed July 28, 2012.
5. Neiman LK, Biller BM, Findling JW et al. The Diagnosis of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2008;93(5):1526-1540.
6. Colao A, Boscaro M, Ferone D et al. Managing Cushing's disease: the state of the art. *Endocrine.* Epub ahead of print 11Jan 2014. DOI 10.1007/s12020-013-0129-2
7. Food and Drug Administration. FDA Drug Safety Communication: FDA limits usage of Nizoral (ketoconazole) oral tablets due to potentially fatal liver injury and risk of drug interactions and adrenal gland problems. Available at <http://www.fda.gov/Drugs/DrugSafety/ucm362415.htm> (Accessed March 6, 2025).
8. Brown DR, Honey EE, Eilerman BS, et al. Clinical management of patients with Cushing syndrome treated with mifepristone: consensus recommendations. *Clinical Diabetes and Endocrinology.* 2020; 6(18).
9. Fleseriu M, Auchus R, Bancos R, et al. Consensus on diagnosis and management of Cushing's disease: a guideline update. *Lancet Diabetes & Endocrinology.* 2021; 9(12):847-875.