VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

KORLYM™ (mifepristone)

Effective Date: 7/24/12
Date Developed: 7/3/12 by Albert Reeves MD
Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19
(Archived 1/22/19)

KORLYM™ is an abortifacient; antineoplastic agent, hormone antagonist; antiprogestin; cortisol receptor blocker

Pre-Authorization Criteria:

VCHCP will authorize KORLYM™ for FDA indicated use to control high blood sugar levels in adult patients with endogenous Cushing's syndrome who have type 2 diabetes or glucose intolerance who have not responded to prior surgery or who are not candidates for surgery.

VCHCP requires that KORLYM™ be prescribed by an **Endocrinologist.**

Dosing: Adult
The recommended starting dose of KORLYM™ is 300 mg once daily. Based on clinical response and tolerability, the dose can be increased in 300 mg increments to a maximum of 1200 mg once daily.

Hyperglycemia in patients with Cushing's syndrome (Korlym™): Oral: Initial dose: 300 mg once daily. Dose may be increased in 300 mg increments at intervals of ≥2-4 weeks based on tolerability and symptom control. Maximum dose: 1200 mg once daily, not to exceed 20 mg/kg/day. If treatment is interrupted, reinitiate at 300 mg/day or a dose lower than the dose that caused the treatment to be stopped if interruption due to adverse reactions

Dosage adjustment with concurrent use of strong CYP450 inhibitor therapy (eg ketoconazole): Maximum dose 300 mg/day

Dosage Forms: U.S.

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Tablet, oral: Korlym™: 300 mg

Prescribing and Access Restrictions

Korlym™ is only available through a restricted access program. For prescriber registration and patient enrollment forms, please refer to https://www.korlymspark.com/login.aspx?ReturnUrl=%2fdefault.aspx or call 1-855-4Korlym (1-855-456-7596).

Administration

Hyperglycemia in patients with Cushing's syndrome: Administer as a single daily dose with a meal. Tablets should be swallowed whole, not crushed, split, or chewed.

Use

Korlym™: To control hyperglycemia occurring secondary to hypercortisolism in patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and who failed surgery or who are not surgical candidates

Adverse Reactions Significant

Adverse events associated with treatment of hyperglycemia in patients with Cushing's syndrome:

>10%:

Cardiovascular: Peripheral edema (26%), hypertension (24%)

Central nervous system: Fatigue (48%), headache (44%), dizziness (22%), pain (14%)

Endocrine & metabolic: Hypokalemia (34% to 44%), endometrial hypertrophy (38%), thyroid function tests abnormal (18%)

Gastrointestinal: Nausea (48%), vomiting (26%), appetite decreased (20%), xerostomia (18%), diarrhea (12%)

Genitourinary: Vaginal bleeding (14%)

Neuromuscular & skeletal: Arthralgia (30%), back pain (16%), myalgia (14%), extremity pain (12%)

Respiratory: Dyspnea (16%), sinusitis (14%), nasopharyngitis (12%)

5% to 10%:

Cardiovascular: Edema, pitting edema

Central nervous system: Anxiety (10%), somnolence (10%), insomnia, malaise

Endocrine & metabolic: Hypoglycemia, triglycerides increased

Gastrointestinal: Anorexia (10%), constipation (10%), abdominal pain, GI reflux

Genitourinary: Vaginal hemorrhage, metrorrhagia

Neuromuscular & skeletal: Flank pain, malaise, musculoskeletal chest pain, weakness

Miscellaneous: Thirst

<5% or frequency not defined: Adrenal insufficiency (4%), pruritus (4%), rash (4%), HDL cholesterol decreased

Warnings/Precautions

Concerns related to adverse effects:

- Adrenal insufficiency: When used for the treatment of hyperglycemia in patients with Cushing's syndrome, adrenal insufficiency may occur. Serum cortisol concentrations remain elevated and may increase, and cannot be used for monitoring. If signs and symptoms of adrenal insufficiency occur (eg, fatigue, hypoglycemia, hypotension, nausea, weakness), discontinue mifepristone and administer glucocorticoids (high doses may be needed). Following resolution, treatment may be resumed at a lower dose; evaluate patient for precipitating causes (eg, infection, trauma).

- Hypokalemia: May occur at any time during therapy when used to control hyperglycemia in patients with Cushing's syndrome. Correct hypokalemia prior to initiation of treatment; monitor potassium levels closely with therapy.

- QT prolongation: May prolong the QT_c interval (dose related); use caution with other QT-prolonging agents.

Disease-related concerns:

- Diabetes: Safety and efficacy have not been established for use in insulin-dependent diabetes mellitus.

- Renal impairment: In patients with severe renal impairment, exposure to mifepristone and its metabolites was increased and a large variability in exposure was observed following multiple doses used in patients with Cushing's syndrome.

REFERENCES

1. Johanssen S and Allolio B, "Mifepristone (RU 486) in Cushing's Syndrome," *Eur J Endocrinol*, 2007, 157(5):561-9. [PubMed 17984235]
2. Spitz IM and Bardin CW, "Mifepristone (RU486) - A Modulator of Progestin and Glucocorticoid Action," *N Engl J Med*, 1993, 329(6):404-12. [PubMed 8326975]

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