HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use KORLYM® safely and effectively. See full prescribing information for KORLYM®.
KORLYM® (mifepristone) 300 mg Tablets
Initial U.S. Approval 2000

WARNING: TERMINATION OF PREGNANCY

See full prescribing information for complete boxed warning.

Mifepristone has potent antiprogestational effects and will result in the termination of pregnancy. Pregnancy must therefore be excluded before the initiation of treatment with KORLYM, or if treatment is interrupted for more than 14 days in females of reproductive potential.

----------RECENT MAJOR CHANGES----------

Dosage and Administration (2.4)	05/2017
Warnings and Precautions (5.6)	05/2017

----------INDICATIONS AND USAGE----------

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 (1).

- **Important Limitations of Use:** Do not use for the treatment of type 2 diabetes mellitus unrelated to endogenous Cushing's syndrome.

----------DOSAGE AND ADMINISTRATION----------

- Administer once daily orally with a meal (2.1).
- The recommended starting dose is 300 mg once daily (2.1).
- Based on clinical response and tolerability, the dose may be increased in 300 mg increments to a maximum of 1200 mg once daily. Do not exceed 20 mg/kg per day (2.1).
- Renal impairment: do not exceed 600 mg once daily (2.2).
- Mild-to-moderate hepatic impairment: do not exceed 600 mg once daily. Do not use in severe hepatic impairment (2.3).
- Concomitant administration with strong CYP3A inhibitors: Do not exceed 600 mg once daily (2.4).

----------DOSAGE FORMS AND STRENGTHS----------

Tablets: 300 mg (3)

----------CONTRAINDICATIONS----------

- Pregnancy (4.1, 8.1)
- Use of simvastatin or lovastatin and CYP3A substrates with narrow therapeutic range (4.2)
- Concurrent long-term corticosteroid use (4.3)
- Women with history of unexplained vaginal bleeding (4.4)
- Women with endometrial hyperplasia with atypia or endometrial carcinoma (4.4)

----------WARNINGS AND PRECAUTIONS----------

- *Adrenal insufficiency*: Patients should be closely monitored for signs and symptoms of adrenal insufficiency (5.1).
- *Hypokalemia*: Hypokalemia should be corrected prior to treatment and monitored for during treatment (5.2).
- *Vaginal bleeding and endometrial changes*: Women may experience endometrial thickening or unexpected vaginal bleeding. Use with caution if patient also has a hemorrhagic disorder or is on anti-coagulant therapy (5.3).
- *QT interval prolongation*: Avoid use with QT interval-prolonging drugs, or in patients with potassium channel variants resulting in a long QT interval (5.4).
- *Use of Strong CYP3A Inhibitors:* Concomitant use can increase mifepristone plasma levels. Use only when necessary and limit mifepristone dose to 600 mg (5.6).

----------ADVERSE REACTIONS----------

Most common adverse reactions in Cushing's syndrome (≥ 20%): nausea, fatigue, headache, decreased blood potassium, arthralgia, vomiting, peripheral edema, hypertension, dizziness, decreased appetite, endometrial hypertrophy (6).

To report suspected adverse reactions, contact Corcept Therapeutics at 1-855-844-3270 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------DRUG INTERACTIONS----------

- Drugs metabolized by CYP3A: Administer drugs that are metabolized by CYP3A at the lowest dose when used with KORLYM (7.1).
- CYP3A inhibitors: Caution should be used when KORLYM is used with strong CYP3A inhibitors. Limit mifepristone dose to 600 mg per day when used with strong CYP3A inhibitors (7.2).
- CYP3A inducers: Do not use KORLYM with CYP3A inducers (7.3).
- Drugs metabolized by CYP2C8/2C9: Use the lowest dose of CYP2C8/2C9 substrates when used with KORLYM (7.4).
- Drugs metabolized by CYP2B6: Use of KORLYM should be done with caution with bupropion and efavirenz (7.5).
- Hormonal contraceptives: Do not use with KORLYM (7.6).

----------USE IN SPECIFIC POPULATIONS----------

- Nursing mothers: Discontinue drug or discontinue nursing (8.3).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 05/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: TERMINATION OF PREGNANCY

Mifepristone is a potent antagonist of progesterone and cortisol via the progesterone and glucocorticoid (GR-II) receptors, respectively. The antiprogestational effects will result in the termination of pregnancy. Pregnancy must therefore be excluded before the initiation of treatment with KORLYM and prevented during treatment and for one month after stopping treatment by the use of a non-hormonal medically acceptable method of contraception unless the patient has had a surgical sterilization, in which case no additional contraception is needed. Pregnancy must also be excluded if treatment is interrupted for more than 14 days in females of reproductive potential.

1 INDICATIONS AND USAGE

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.

LIMITATIONS OF USE:

- KORLYM should not be used in the treatment of patients with type 2 diabetes unless it is secondary to Cushing's syndrome.

2 DOSAGE AND ADMINISTRATION

2.1 Adult Dosage

The recommended starting dose is 300 mg orally once daily. KORLYM must be given as a single daily dose. KORLYM should always be taken with a meal. Patients should swallow the tablet whole. Do not split, crush, or chew tablets.

Dosing and titration

The daily dose of KORLYM may be increased in 300 mg increments. The dose of KORLYM may be increased to a maximum of 1200 mg once daily but should not exceed 20 mg/kg per day. Increases in dose should not occur more frequently than once every 2-4 weeks. Decisions about dose increases should be based on a clinical assessment of tolerability and degree of improvement in Cushing's syndrome manifestations. Changes in glucose control, anti-diabetic medication requirements, insulin levels, and psychiatric symptoms may provide an early assessment of response (within 6 weeks) and may help guide early dose titration. Improvements in cushingoid appearance, acne, hirsutism, striae, and body weight occur over a longer period of time and, along with measures of glucose control, may be used to determine dose changes beyond the first 2 months of therapy. Careful and gradual titration of KORLYM accompanied by monitoring for recognized adverse reactions (*See Warnings and Precautions 5.1 and 5.2*) may reduce the risk of severe adverse reactions. Dose reduction or even dose discontinuation may be needed in some clinical situations. If KORLYM treatment is interrupted, it should be reinitiated at the lowest dose (300 mg). If treatment was interrupted because of adverse reactions, the titration should aim for a dose lower than the one that resulted in treatment interruption.

2.2 Dosing in Renal Impairment

No change in initial dose of KORLYM is required in renal impairment. The maximum dose should be limited to 600 mg. *[See Renal Impairment (8.6) and Clinical Pharmacology (12.3)]*

2.3 Dosing in Hepatic Impairment

No change in the initial dose of KORLYM is required in mild to moderate hepatic impairment. The maximum dose should be limited to 600 mg. KORLYM should not be used in severe hepatic impairment. *[See Hepatic Impairment (8.7) and Clinical Pharmacology (12.3)]*

2.4 Concomitant Administration with CYP3A Inhibitors

Ketoconazole and other strong inhibitors of CYP3A, such as itraconazole, nefazodone, ritonavir, nelfinavir, indinavir, atazanavir, amprenavir and fosamprenavir, clarithromycin, conivaptan, lopinavir/ritonavir, posaconazole, saquinavir, telithromycin, or voriconazole may increase exposure to mifepristone. KORLYM should be used in combination with strong CYP3A inhibitors only when necessary. [See Warnings and Precautions (5.6), Drug Interactions (7.2)]

Administration of KORLYM to patients already being treated with strong CYP3A inhibitors:

- Start at a dose of 300 mg. If clinically indicated, titrate to a maximum of 600 mg.

Administration of strong CYP3A inhibitors to patients already being treated with KORLYM:

- Adjust the dose of KORLYM according to Table 1.

Table 1. Dose adjustment of KORLYM when strong CYP3A inhibitor is added

Current dose of KORLYM	Adjustment to dose of KORLYM if adding a strong CYP3A inhibitor
300 mg	No change
600 mg	Reduce dose to 300 mg. If clinically indicated, titrate to a maximum of 600 mg
900 mg	Reduce dose to 600 mg
1200 mg	Reduce dose to 600 mg

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3 DOSAGE FORMS AND STRENGTHS

Tablets: 300 mg

Oval shaped, light yellow to yellow tablets debossed with “Corcept” on one side and “300” on the other side. The tablets are not scored.

4 CONTRAINDICATIONS

4.1 Pregnancy

KORLYM is contraindicated in women who are pregnant. Pregnancy must be excluded before the initiation of treatment with KORLYM or if treatment is interrupted for more than 14 days in females of

reproductive potential. Non-hormonal contraceptives should be used during and one month after stopping treatment in all women of reproductive potential. *[See Use in Specific Populations 8.8]*

4.2 Drugs Metabolized by CYP3A

KORLYM is contraindicated in patients taking simvastatin, lovastatin, and CYP3A substrates with narrow therapeutic ranges, such as cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus, due to an increased risk of adverse events. *[See Drug Interactions (7.1) and Clinical Pharmacology (12.3)]*

4.3 Corticosteroid Therapy Required for Lifesaving Purposes

KORLYM is contraindicated in patients who require concomitant treatment with systemic corticosteroids for serious medical conditions or illnesses (e.g., immunosuppression after organ transplantation) because KORLYM antagonizes the effect of glucocorticoids.

4.4 Women with Risk of Vaginal Bleeding or Endometrial Changes

KORLYM is contraindicated in the following:

- Women with a history of unexplained vaginal bleeding
- Women with endometrial hyperplasia with atypia or endometrial carcinoma

4.5 Known Hypersensitivity to Mifepristone

KORLYM is contraindicated in patients with prior hypersensitivity reactions to mifepristone or to any of the product components.

5 WARNINGS AND PRECAUTIONS

5.1 Adrenal Insufficiency

Patients receiving mifepristone may experience adrenal insufficiency. Because serum cortisol levels remain elevated and may even increase during treatment with KORLYM, serum cortisol levels do not provide an accurate assessment of hypoadrenalism in patients receiving KORLYM. Patients should be closely monitored for signs and symptoms of adrenal insufficiency, including weakness, nausea, increased fatigue, hypotension, and hypoglycemia. If adrenal insufficiency is suspected, discontinue treatment with KORLYM immediately and administer glucocorticoids without delay. High doses of supplemental glucocorticoids may be needed to overcome the glucocorticoid receptor blockade produced by mifepristone. Factors considered in deciding on the duration of glucocorticoid treatment should include the long half-life of mifepristone (85 hours).

Treatment with KORLYM at a lower dose can be resumed after resolution of adrenal insufficiency. Patients should also be evaluated for precipitating causes of hypoadrenalism (infection, trauma, etc.).

5.2 Hypokalemia

In a study of patients with Cushing's syndrome, hypokalemia was observed in 44% of subjects during treatment with KORLYM. Hypokalemia should be corrected prior to initiating KORLYM. During KORLYM administration, serum potassium should be measured 1 to 2 weeks after starting or increasing the dose of KORLYM and periodically thereafter. Hypokalemia can occur at any time during KORLYM

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