mifepristone (mi-fe-pris-tone)

Classification
Therapeutic: antiprogestational agents
Pharmacologic: antiprogestational agents

Pregnancy Category
B (Mifeprex), X (Korlym)

Indications
Mifeprex: Medical termination of intrauterine pregnancy up to day 49 of pregnancy.
Korlym: Anticancer therapy for patients with Cushing’s syndrome who have type 2 diabetes or glucose intolerance and have failed or are not candidates for surgery.

Action
Antagonizes endometrial and myometrial effects of progesterone. Sensitizes the myometrium to contraction-inducing activity of prostaglandins. Antagonizes the glucocorticoid receptor.

Therapeutic Effects: Termination of pregnancy. Improved control of blood glucose.

Pharmacokinetics

- Absorption: Rapidly absorbed following oral administration (69% bioavailability).
- Distribution: Unknown.
- Protein Binding: 98%.
- Elimination:
  - Metabolism: Mostly metabolized by the liver (CYP3A4 enzyme system).
  - Excreted in the feces.
- Half-life: 18 hr.

TIME/ACTION PROFILE (termination of pregnancy)

- PO: unknown within 2 days unknown

Contraindications/Precautions

- Contraindicated in:
  - Hypersensitivity; Presence of an intrauterine device (IUD)
  - OB: Confirmed or suspected ectopic pregnancy (Mifeprex); Undiagnosed adnexal mass (Mifeprex); Chronic adrenal failure (Mifeprex); Concurrent long-term corticosteroid therapy.
  - Bleeding disorders or concurrent anticoagulant therapy (Mifeprex).
  - Idiopathic porphyrias (Mifeprex).
  - Severe hepatic impairment (Korlym).
  - OB: Inherited porphyrias (Mifeprex); Severe hepatic impairment (Korlym); Severe renal impairment (Korlym).
  - Severe hepatic impairment (Mifeprex); Concurrent use with simvastatin, lovastatin, cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, or telaprevir (Korlym).
  - Use Cautiously in:
    - Women ≥ 35 yrs old or who smoke ≥ 10 cigarettes/day (Mifeprex).
    - Chronic medical conditions such as cardiovascular, hypertensive, hepatic, renal, or respiratory disease (safety and efficacy not established) (Mifeprex).
    - Exercise Extreme Caution in:
      - Women > 35 yrs old or who smoke ≥ 10 cigarettes/day (Mifeprex).
      - Women > 50 yrs old.

Adverse Reactions/Side Effects

- CNS:
  - Headache, dizziness
  - Anxiety (Korlym)
  - Sleep disorders (Korlym)
  - Insomnia (Korlym)
  - Rash
  - Nervousness
  - QT interval prolongation (Korlym)
  - Hyperglycemia (Korlym)

- CV:
  - Hypotension (Korlym)
  - Hypertension (Korlym)

- Derm:
  - Rash
  - Urticaria
  - Hypersensitivity reactions (Korlym)

- GI:
  - Diarrhea (Mifeprex)
  - Diarrhea (Korlym)
  - Dyspepsia (Korlym)
  - Nausea (Korlym)
  - Vomiting (Korlym)

- GU:
  - Urethritis (Korlym)
  - Dysuria (Korlym)
  - Vaginal bleeding

- Endo:
  - Endometrial hyperplasia with atypia or endometrial carcinoma (Korlym)

- MS:
  - Myalgia (Korlym)

- Resp:
  - Dyspnea (Korlym)
  - Pneumonia (Korlym)

- F and E:
  - Hypokalemia (Korlym)
  - Hypothyroidism (Korlym)
  - Hypocalcemia (Korlym)

- Local:
  - Vaginal bleeding

- Other:
  - Hyperglycemia secondary to hypercortisolism in patients with endogenous Cushing’s syndrome who have type 2 diabetes or glucose intolerance and have failed or are not candidates for surgery.
  - Exercise Extreme Caution in:
    - Women > 35 yrs old or who smoke ≥ 10 cigarettes/day (Mifeprex).
    - Women > 50 yrs old.

Interactions

- Drug-Drug:
  - Mifepristone is a substrate and inhibitor of the CYP3A4 enzyme system.
  - Strong CYP3A4 inhibitors or inducers may alter mifepristone levels; extreme caution with concurrent use of dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, or telaprevir.
  - Strong CYP3A4 inhibitors may increase mifepristone levels; caution with concurrent use of mifepristone.
  - Concurrent use with moderate CYP3A4 inhibitors; Bleeding disorders or concurrent anticoagulant therapy (Korlym).

  - Concurrent use with strong CYP3A4 inhibitors (Korlym).

Concurrent use with strong CYP3A4 inhibitors

- Drug-Laboratory Tests:
  - Serum potassium levels; extreme caution with concurrent use of dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, or telaprevir.
  - Serum potassium levels; caution with concurrent use of mifepristone.

- Pregnancy Risk Factor: X

- Lactation: Avoid.


- REMS
  - OB: Pregnancy (Mifeprex), pelvic pain (Mifeprex).
  - OB: Pregnant women (Mifeprex); Women > 50 yrs old.

- MD:
  - MD: Pregnancy (Mifeprex), pelvic pain (Mifeprex).

- CONC: Administer to women who are not pregnant; women of childbearing age must use effective contraception during and for at least 4 wk after treatment.

Pharmacologic/Synergistic:
- antiprogestational agents
- abortifacients, antidiabetics

Classification
- antiprogestational agents

Pregnancy Category
- UK (Mifeprex), X (Korlym)

Pharmacologic:
- antiprogestational agents

Therapeutic:
- abortifacients, antidiabetics
Korlym. Blood levels and effects may be increased by rifampin, rifabutin, dexamethasone, phenytoin, phenobarbital, and carbamazepine; avoid concurrent use with Korlym.

Drug-Natural Products: Blood levels and effects may be increased by St. John’s wort; avoid concurrent use with Korlym.

Drug-Food: Blood levels and effects may be increased by grapefruit juice; caution with concurrent use of Korlym.

Route/Dosage

Mifepristone
PO (Adults): 10 mg, 25 mg, 50 mg once daily; may be increased every 2–4 wk (maximum dose: 300 mg/day). Concurrent strong CYP3A4 inhibitor therapy—10 mg once daily (maximum dose: 300 mg/day).

Korlym
PO (Adults): 300 mg once daily; may be increased every 2–4 wk (maximum dose: 1200 mg/day or 20 mg/kg/day).

Renal Impairment
PO (Adults): 300 mg once daily; may be increased every 2–4 wk (maximum dose: 600 mg/day).

Hepatic Impairment
PO (Adults): 300 mg once daily; may be increased every 2–4 wk (maximum dose: 600 mg/day).

NURSING IMPLICATIONS

Assessment

Mifepristone: Determine duration of pregnancy. Pregnancy is dated from the first day of the last menstrual period in a presumed 28-day cycle with ovulation occurring at midcycle and can be determined by menstrual history and clinical examination, or ultrasonographic determination if ovulatory pregnancy is suspected.

Monitor amount of bleeding and cramping during treatment. Determine if termination of pregnancy has occurred on day 14.

Korlym: Monitor for changes in Cushingoid appearance (acne, hirsutism, striae, body weight) during therapy.

Monitor for signs and symptoms of adrenal insufficiency (weakness, nausea, increased fatigue, hypotension, hypoglycemia) during therapy. If adrenal insufficiency is suspected, discontinue Korlym and administer glucocorticoids immediately.

Lab Test Considerations: Mifepristone: hemoglobin, hematocrit, and BUN may occur in women who bleed heavily.

Changes in quantitative human chorionic gonadotropin (hCG) levels are not accurate until at least 10 days after mifepristone administration; complete termination of pregnancy may be confirmed by clinical examination.

Korlym: Correct hypokalemia prior to initiating therapy. Assess serum potassium 1–2 wk after starting or increasing dose of Korlym and periodically thereafter.

Obtain a negative pregnancy test in women prior to starting therapy or before resuming therapy if stopped for more than 14 days.

Monitor Hemoglobin A1c periodically during therapy.

Potential Nursing Diagnoses

Acute pain (Side Effects)

Deficient knowledge, related to medication regimen (Patient/Family Teaching)

Implementation

Do not confuse mifepristone with misoprostol.

Mifepristone: Mifepristone should be administered only by health care professionals who have read and understood the prescribing information, are able to assess gestational age of an embryo and diagnose ectopic pregnancies, and who are able to provide surgical intervention in cases of incomplete abortion or severe bleeding.

Any IUD should be removed prior to mifepristone administration.

Measures to prevent rhesus immunization, similar to those of surgical abortion, should be taken.

PO (Adults): after the patient has read the Medication Guide and signed the Patient Agreement, administer three 200 mg tablets of mifepristone as a single dose. On day 3, unless abortion has occurred and been confirmed by clinical examination or ultrasound, administer two 200-mcg tablets of misoprostol. On day 14, confirm that termination of pregnancy has occurred by clinical examination or ultrasound.

Korlym: Administer with a meal. Swallow tablet whole; do not crush, break, or chew.

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mifepristone

If Korlym therapy is interrupted, reinitiate at lowest dose (300 mg).

Patient/Family Teaching

- **Mifeprex**: Advise patient of the treatment and its effects. Patient must be given a copy of the Medication Guide and Patient Agreement. Patient must understand the necessity of completing the treatment schedule of three office visits (day 1, day 3, and day 14).

- Inform patient that vaginal bleeding and intense cramping will probably occur and that prolonged or heavy vaginal bleeding is not proof of complete expulsion. Bleeding or spotting occurs for an average of 9–16 days, but may continue for more than 30 days. Advise patient that if the treatment fails, there is a risk of fetal malformation; medical abortion failures are managed by surgical termination.

- Caution patient to notify health care professional immediately if she develops weakness, nausea, vomiting, diarrhea, with or without abdominal pain or fever more than 24 hr after taking mifepristone: may indicate life-threatening sepsis.

- Instruct patient in the steps to take in an emergency situation, including precise instructions and a telephone number to call if the has problems or concerns.

- May cause dizziness or fainting. Caution patient to avoid driving or other activities requiring alertness until response to medication is known.

- Caution patient to avoid drinking grapefruit juice during therapy; may increase risk of side effects.

- Instruct patient to notify health care professional if signs and symptoms of adrenal insufficiency, abnormal vaginal bleeding, or low potassium (muscle weakness, aches, cramps, palpitations) occur.

- Advise patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken and to consult with health care professional before taking other medications.

- Advise female patient to use a nonhormonal form of contraception during and for at least 1 month after therapy. Notify health care professional immediately if pregnancy is suspected; Korlym is teratogenic. Advise female patient to avoid breast feeding during therapy.

Evaluation/Desired Outcomes

- **Mifeprex**: Termination of an intrauterine pregnancy of less than 49 days' duration.

- **Korlym**: Improved control of blood glucose.

Why was this drug prescribed for your patient?