ketoconazole (systemic)† (kee-toe-koe-na-zole)

**Natural**

**Classification**
Therapeutic: antifungals (systemic)

**Pregnancy Category** C

**Therapeutic Action**
• Interferes with fungal metabolism
• Inhibits the production of adrenal steroids
• Disrupts fungal cell membrane

**Indications**
Treatment of Candidiasis (dissminated and esophageal), Chromomycosis, Coccidiodomycosis, Blastomycosis, Paracoccidioidomycosis. Ketoconazole should only be used when other effective antifungal therapy is NOT available AND the potential benefits of oral ketoconazole outweigh its potential risks.

**Half-life:** 8 hr.

**PO** rapid 1–4 hr 24 hr

**Absorption from the GI tract is pH dependent; increasing pH decreases absorption.**

**Pharmacokinetics**
- **Metabolism and Excretion:** Crosses the placenta; enters breast milk.
- **Protein Binding:** 99%
- **Distribution:** Widely distributed. CNS penetration is unpredictable and minimal. Absorption from the GI tract is pH dependent; increasing pH decreases absorption.

**Pharmacodynamics**
- **Absorption:** Absorption from the GI tract is pH dependent; increasing pH decreases absorption.

**Spectrum:** Active against many pathogenic fungi, including:
- Coccidioides immitis
- Histoplasma capsulatum
- Cryptococcus neoformans
- Blastomyces dermatitidis
- Aspergillus
- Candida
- Malassezia
- Trichophyton
- Microsporum

**Use Cautiously in:** History of liver disease; Achlorhydria or hypochlorhydria; Alcoholism; Adrenal insufficiency; Concurrent dofetilide, quinidine, and战ines; Concurrent use with alcohol.

**Contraindications/Precautions**
- **Contraindicated in:** Hyper sensitive; Liver disease. Concurrent use with potent CYP3A4 inhibitors (e.g., ritonavir, indinavir, saquinavir, telithromycin). Concurrent use with cytochrome P450 (CYP) inhibitors. Concurrent use with disulfiram.

**Patient Teaching**
- Use w/meal if GI distress occurs
- Continue indefinitely

**Adverse Reactions/Side Effects**
- **CNS:** dizziness, drowsiness.
- **CV:** torsades de pointes, Q tetral prolonged.
- **GI:** nausea, vomiting, diarrhea, flatulence.
- **GU:** dysuria, oligospermia.
- **Derm:** rash, pruritus, acne, alopecia, gynecomastia.
- **EENT:** photophobia.
- **Endo:** adrenal insufficiency, hypergonadism, male hypogonadism.
- **Respiratory:** bronchospasm.
- **Misc:** rash, pruritus, arthralgia, fatigue.

**Drug Interactions**
- **Effects on other drugs:**
  - May significantly increase serum levels and risk of toxicity with nisoldipine, niacin, and cyclosporine; concurrent use contraindicated. May significantly decrease serum levels of lordipine and risk of myopathy with lordipine; concurrent use contraindicated. May significantly increase levels of propranolol, meprobamate, valproic acid, and quinidine; concurrent use contraindicated. May significantly decrease levels of calcium-channel blockers and warfarin; concurrent use contraindicated. May significantly decrease levels of anticoagulants and risk of bleeding; concurrent use contraindicated. May significantly increase serum levels of methotrexate and risk of toxicity; concurrent use contraindicated.
- **Effects on ketoconazole:**
  - May significantly decrease levels of methotrexate and risk of toxicity; concurrent use contraindicated. May significantly increase levels of methotrexate and risk of toxicity; concurrent use contraindicated. May significantly decrease levels of methotrexate and risk of toxicity; concurrent use contraindicated. May significantly decrease levels of methotrexate and risk of toxicity; concurrent use contraindicated.

**Air-Drug:**
- May significantly increase levels of methotrexate and risk of toxicity; concurrent use contraindicated. May significantly decrease levels of methotrexate and risk of toxicity; concurrent use contraindicated. May significantly decrease levels of methotrexate and risk of toxicity; concurrent use contraindicated. May significantly decrease levels of methotrexate and risk of toxicity; concurrent use contraindicated.

**Monitoring Parameters**
- Monitor for adverse effects and for signs of infection.

**Dosing**
- **Adults:** 200–400 mg PO q 24 hr
- **Children:** PO q 24 hr
- **Note:** Not available in chewable tablets, because of buffer.

**Children:**
- **Pedi:** PO: 2 mg/kg q 24 hr

**Dosage Form(s):**
- Capsules (200 mg, 400 mg, 800 mg, 1600 mg)
- Tablets (200 mg, 400 mg, 800 mg, 1600 mg)
- Oral solution (200 mg/mL)

**Product Information**
- **Canadian drug name:**
- **Generic Implication:**
- **Genetic Implication:**
- **Bibliography:**
- **Hypersensitivity:**
**Route/Dosage**

**PO (Adults):** 200–400 mg/day, single dose.

**PO (Children >2yr):** 3.3–6.6 mg/kg/day, single dose.

**NURSING IMPLICATIONS**

**Assessment**
- Assess patient for symptoms of infection prior to and periodically during therapy.
- Special care for cultures should be taken prior to instituting therapy. Therapy may be started before results are obtained.

**Lab Test Considerations:** Monitor hepatic function tests (SGGT, alkaline phosphatase, ALT, AST, total bilirubin [TB], Prothrombin Time [PT], International Normalization Ratio [INR], and testing for viral hepatitis) prior to therapy. Monitor ALT weekly during therapy; if above normal limits or 30% above baseline, or patient develops symptoms of liver injury, interrupt ketoconazole therapy and obtain full set of liver tests. Repeat tests to ensure normalization of values. If restarting therapy, monitor liver function frequently.
- May cause serum testosterone concentrations.

**Potential Nursing Diagnoses**

- Risk for infection (Indications)
- Noncompliance (Patient/Family Teaching)

**Implementation**
- PO: Administer with meals or snacks to minimize nausea and vomiting.
- Shake suspension well prior to administration.
- Do not administer histamine H2 antagonists or antacids within 2 hr of ketoconazole.
- For patients with achlorhydria, dissolve each tablet in 4 mL of aqueous solution of 0.2 N hydrochloric acid. Use a glass or plastic straw to avoid contact with teeth and follow with a glass of water, swished in mouth and swallowed.

**Patient/Family Teaching**
- Instruct patient to take medication as directed, at the same time each day, even if feeling better. Take missed doses as soon as remembered, if almost time for next dose, space missed dose and next dose 10–12 hr apart.
- Advise patient to avoid concurrent use of alcohol while taking ketoconazole; may cause a disulfiram-like reaction (flushing, rash, peripheral edema, nausea, headache) and increase the risk of hepatotoxicity.
- May cause dizziness or drowsiness. Caution patient to avoid driving or other activities requiring alertness and response to medication is known.
- Advise patients to avoid taking tetracyclines within 1 hr of ketoconazole.
- Caution patient to wear sunglasses and to avoid prolonged exposure to bright light to prevent photophobic reactions.
- Instruct patient to notify health care professional if abdominal pain, fever, or diarrhea becomes pronounced or if signs and symptoms of liver dysfunction (unusual fatigue, anorexia, nausea, vomiting, jaundice, dark urine, or pale stools) occur.
- Advise patient to use a nonhormonal form of contraception during ketoconazole therapy.

**Evaluation/Desired Outcomes**
- Resolution of clinical and laboratory indications of fungal infections.
- Minimal treatment for candidiasis is 1–2 wk and for other systemic mycoses is 6 mo.
- Chronic mucocutaneous candidiasis usually requires maintenance therapy.

**Why was this drug prescribed for your patient?**