**Fluconazole** (flu-ko-naz-ole)

**Class**: Antifungals (systemic)

**Pregnancy Category**: C (single-dose oral treatment of vaginal candidiasis), D (all other indications)

**Indications**
- **PO, IV**: Fungal infections caused by susceptible organisms, including oropharyngeal or esophageal candidiasis, Neoscytalidomycosis, urinary tract infections, and meningitis.
- **PO**: Single-dose oral treatment of vaginal candidiasis.
- **Unlabeled Use**: Prevention of recurrent vaginal yeast infections.

**Action**
- Inhibits synthesis of fungal sterols, a necessary component of the cell membrane.

**Therapeutic Effects**
- Fungistatic action against susceptible organisms. May be fungicidal in higher concentrations.

**Spectrum**
- *Cryptococcus neoformans*.
- *Candida* spp.

**Pharmacokinetics**
- **Absorption**: Well absorbed after oral administration.
- **Distribution**: Widely distributed, good penetration into CSF, saliva, sputum, vaginal fluid, skin, eye, and peritoneum. Excreted in breast milk.
- **Metabolism and Excretion**: 80% excreted unchanged by the kidneys; 10% metabolized by the liver.
- **Half-life**: Premature neonates: 46–74 hr; Children: 19–25 hr (PO) and 15–17 hr (IV); Adults: 30 hr.

**TIME/ACTION PROFILE (blood levels)**

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>unknown</td>
<td>2–4 hr</td>
<td>24 hr</td>
</tr>
</tbody>
</table>

**Contraindications/Precautions**
- **Contraindication**: Hypersensitivity to fluconazole or other azole antifungals.
- **Use Cautionally in**: Renal impairment (dose required if CrCl < 50 mL/min); Abdominal distention, nausea, vomiting.
- **Use Cautiously in**: Renal impairment (dose required if CrCl < 50 mL/min); Underlying liver disease; OB: Safety not established; Congenital defects have occurred with use of high-dose fluconazole (400–800 mg/day).
- **Lactation**: Usually compatible with breast-feeding.
- **Geri**: Risk of adverse reactions (rash, vomiting, diarrhea, seizures); consider age-related risk in determining dose.

**Adverse Reactions/Side Effects**
- **CNS**: Headache, dizziness, seizures.
- **GI**: Hepatotoxicity, abdominal discomfort, diarrhea, nausea, vomiting.
- **Derm**: Exfoliative skin disorders including STEVENS-JOHNSON SYNDROME.
- **Endo**: Hypokalemia, hypertriglyceridemia.
- **Misc**: Allergic reactions, including ANAPHYLAXIS.

**Interactions**
- **Drug-Drug**: May increase activity of warfarin.
- **Rifampin**, **rifabutin**, and **isoniazid** may increase levels of fluconazole at doses >200 mg/day may inhibit the CYP3A4 enzyme system and affect the activity of drugs metabolized by this system.
- Hypoglycemic effects of tolbutamide, glyburide, or glipizide.
- Levels and effects of benzodiazepines, zolpidem, buspirone, nisoldipine, tricyclic antidepressants, and losartan.
- Levels of tofacitinib; dose of tofacitinib to 5 mg once daily. May **QD** risk of bleeding with warfarin.
- May antagonize effects of amphotericin B. May **QD** voriconazole levels; avoid concurrent use.

**Route/Dosage**

**Oropharyngeal Candidiasis**
- **PO, IV (Adults)**: 200 mg initially, then 100 mg daily for at least 2 wk.
- **PO, IV (Children >6 months)**: 4 mg/kg initially, then 3 mg/kg/day for at least 2 wk.
- **PO, IV (Neonates, >4 days; 35–50 weeks gestation)**: same dose as older children except frequency of q 48 hr.
- **Premature neonates; >4 days; gestation; 5–6 mg/kg/dose q 48–72 hr.**

**Esophageal Candidiasis**
- **PO, IV (Adults)**: 200 mg initially, then 100 mg once daily for at least 3 wk (up to 400 mg/day).
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PO, IV (Children >14 days): 6 mg/kg initially, then 5–12 mg/kg/day for at least 3 wk.

PO, IV (Neonates <14 days, 30–36 weeks gestation): same dose as older children except frequency is q 48 hr. Premature neonates: 29 weeks gestation: 5–6 mg/kg/dose q 48–72 hr.

Vaginal Candidiasis
PO (Adults): 150-mg single dose; prevention of recurrence (unlabeled)—150 mg daily for 5–7 days if no symptoms for 6 months.

PO, IV (Children >14 days): 6 mg/kg initially, then 3–12 mg/kg/day for at least 3 wk.

PO, IV (Neonates <14 days, 30–36 weeks gestation): same dose as older children except frequency is q 48 hr. Premature neonates: 29 weeks gestation: 5–6 mg/kg/dose q 48–72 hr.

Systemic Candidiasis
PO, IV (Adults): 200–400 mg/day initially, then 200–800 mg/day for 28 days.

PO, IV (Children >14 days): 6–12 mg/kg/day for 28 days.

PO, IV (Neonates <14 days, 30–36 weeks gestation): same dose as older children except frequency is q 48 hr. Premature neonates: 29 weeks gestation: 5–6 mg/kg/dose q 48–72 hr.

Vaginal Candidiasis
PO (Adults): 150-mg single dose; prevention of recurrence (unlabeled)—150 mg daily for 5–7 days if no symptoms for 6 months.

PO, IV (Children >14 days): 6 mg/kg initially, then 3–12 mg/kg/day for at least 3 wk.

PO, IV (Neonates <14 days, 30–36 weeks gestation): same dose as older children except frequency is q 48 hr. Premature neonates: 29 weeks gestation: 5–6 mg/kg/dose q 48–72 hr.

Cryptococcal Meningitis
PO, IV (Adults): Treatment—400 mg once daily until favorable clinical response, then 200–800 mg once daily.

PO, IV (Children >14 days): 12 mg/kg/day initially, then 6–12 mg/kg/day for at least 10–12 wk after clearing of CSF; change to oral therapy as soon as possible. Suppressive therapy—200 mg once daily.

PO, IV (Neonates <14 days, 30–36 weeks gestation): same dose as older children except frequency is q 48 hr. Premature neonates: 29 weeks gestation: 5–6 mg/kg/dose q 48–72 hr.

Prevention of Candidiasis after Bone Marrow Transplant
PO, IV (Adults): 400 mg once daily; begin several days before procedure if severe neutropenia is expected, and continue for 2–7 days after ANC >/= 1000/mm3.

PO, IV (Children >14 days): 10–12 mg/kg/day, not to exceed 600 mg/day.

Renal Impairment
PO, IV (Adults): CCr 11–50 mL/min—50% of the usual dose.

NURSING IMPLICATIONS
Assessment

- Assess infected area and monitor CSF cultures before and periodically during therapy.
- Specimens for cultures should be taken before instituting therapy. Therapy may be started before results are obtained.

- Assess patient for rash (mild to moderate rash usually occurs in the 2nd wk of therapy and resolves within 1–2 wk of continued therapy). If rash is severe (excessive erythema or maculopapular rash with intense desquamation or angioedema) or accompanied by systemic symptoms (serum sickness-like reaction, Stevens-Johnson syndrome, toxic epidermal necrolysis), therapy must be discontinued immediately.

- Lab Test Considerations: Monitor renal function tests before and periodically during therapy. Patients with renal dysfunction will require dose adjustment.

Potential Nursing Diagnoses
Risk for infection (Indications)

Implementation

- Do not confuse Diflucan (fluconazole) with Diprivan (propofol).

IV Administration

- Intravenous Infusion: Diluent: Premixed infusions are pre-diluted and ready to use. Do not administer solution that is cloudy or has a precipitate. Check for leaks by squeezing inner bag. If leaks are found, discard container as unsterile. Concentration: 2 mg/mL. Rate: Infuse over 1–2 hr. Do not exceed a rate of 200 mg/hr. Ped: For children receiving doses >6 mg/kg/day, give over 2 hr.

- Y-Site Compatibility: acyclovir, abedaciclib, abemaciclib, alexicabtagene, alemtuzumab, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisib, alpelisiba...
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**Patient/Family Teaching**

- Instruct patient to take medication as directed, even if feeling better. Doses should be taken at the same time each day. Take missed doses as soon as remembered, but not if almost time for next dose. Do not double doses.

- Instruct patient to notify health care professional if skin rash, abdominal pain, fever, or diarrhea becomes pronounced, if signs and symptoms of liver dysfunction (unusual fatigue, anorexia, nausea, vomiting, jaundice, dark urine, or pale stools) occur, if unusual bruising or bleeding occurs, or if no improvement is seen within a few days of therapy.

**Evaluation/Desired Outcomes**

- Resolution of clinical and laboratory indicators of fungal infections. Full course of therapy may require weeks or months of treatment after resolution of symptoms.

- Prevention of candidiasis in patients who have undergone bone marrow transplantation.

- Decrease in skin irritation and vaginal discomfort in patients with vaginal candidiasis. Diagnosis should be reconfirmed with smears or cultures before a second course of therapy to rule out other pathogens associated with vulvovaginitis. Recurrent vaginal infections may be a sign of systemic illness.

Why was this drug prescribed for your patient?

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buprenorphine, butorphanol, calcium chloride, carboplatin, carmustine, caspofungin, cefazolin, cefepime, cefoperazone, cefotetan, cefoxitin, ceftaroline, chlorpromazine, cisatracurium, cisplatin, cyanocobalamin, cyclophosphamide, cyclosporine, cytarabine, dacarbazine, dexamethasone sodium phosphate, dexmedetomidine, doxorubicin, doxycycline, drotrecogin alfalfa, etoposide, epinephrine, eprosartan, eptifibatide, erythromycin, esmolol, etoposide, etoposide phosphate, famotidine, fenoldopam, fentanyl, filgrastim, fludarabine, fluorouracil, folic acid, foscarnet, ganciclovir, gemcitabine, gentamicin, glycopyrrolate, granisetron, heparin, hydrocortisone, hydromorphone, idarubicin, ifosfamide, immune globulin IV, indomethacin, insulin, irinotecan, isoproterenol, ketorolac, labetolol, leucovorin, levofloxacin, lidocaine, linezolid, lorazepam, magnesium sulfate, mannitol, mechlorethamine, melphalan, meperidine, meropenem, metaraminol, methotrexate, methyldopate, methylprednisolone sodium succinate, metoclopramide, metoprolol, metronidazole, midazolam, milrinone, mitoxantrone, morphine, multivitamins, mycophenolate, nafcillin, nalbuphine, naloxone, nesiritide, nicardipine, nitroglycerin, nitroprusside, norepinephrine, octreotide, ondansetron, oxacillin, oxaliplatin, oxytocin, paclitaxel, palonosetron, pamidronate, pancuronium, papaverine, pentazocine, pentobarbital, phenobarbital, phentolamine, phenylephrine, phytonadione, piperacillin/tazobactam, potassium acetate, potassium chloride, procainamide, prochlorperazine, promethazine, propylthiouracil, propranolol, propranolol hydrochloride, psoralen, quinupristin-dalfopristin, ranitidine, remifentanil, rituximab, rocuronium, sargramostim, sodium acetate, sodium bicarbonate, streptokinase, succinylcholine, sufentanil, tacrolimus, telavancin, teniposide, theophylline, thiotepa, ticarcillin/clavulanate, tigecycline, tirofiban, tobramycin, tolazoline, trastuzumab, vancomycin, vasopressin, vecuronium, verapamil, vinblastine, vincristine, vinorelbine, voriconazole, zidovudine, zoledronic acid.