Diflucan (fluconazole) - Drug Summary

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Diflucan Oral (fluconazole)

THERAPEUTIC CLASS

Azole antifungal

DEA CLASS

RX

ADULT DOSAGE & INDICATIONS

Prophylaxis in Bone Marrow Transplant

Decrease Incidence of Candidiasis:
400mg qd

Start prophylaxis several days before the anticipated onset of neutropenia in patients who are anticipated to have severe granulocytopenia (<500 neutrophils/mm^3); continue for 7 days after the neutrophil count rises >1000 cells/mm^3

Cryptococcal Meningitis

400mg on 1st day, followed by 200mg qd for 10-12 weeks after the CSF becomes culture (-); a dose of 400mg qd may be used

Suppression of Cryptococcal Meningitis Relapse in AIDS:
200mg qd

Vaginal Candidiasis

PO Single Dose:
150mg

Oropharyngeal Candidiasis

200mg on 1st day, followed by 100mg qd for ≥2 weeks

Esophageal Candidiasis

200mg on 1st day, followed by 100mg qd for a minimum of 3 weeks and for ≥2 weeks following resolution of symptoms
Doses up to 400mg/day may be used

Candida Infections

Systemic Infections:
Max: 400mg qd

UTIs/Peritonitis:
50-200mg/day

PEDIATRIC DOSAGE & INDICATIONS

Cryptococcal Meningitis

12mg/kg on 1st day, followed by 6mg/kg qd for 10-12 weeks after the CSF becomes culture (-); a dose of 12mg/kg qd may be used (not to exceed 600mg/day)

Suppression of Cryptococcal Meningitis Relapse in AIDS:
6mg/kg qd

Candida Infections

Systemic:
6-12mg/kg/day (not to exceed 600mg/day)

Esophageal Candidiasis

6mg/kg on 1st day, followed by 3mg/kg qd for a minimum of 3 weeks and for ≥2 weeks following resolution of symptoms; doses up to 12mg/kg/day may be used (not to exceed 600mg/day)

Oropharyngeal Candidiasis

6mg/kg on 1st day, followed by 3mg/kg qd for ≥2 weeks

DOSING CONSIDERATIONS

Renal Impairment
Multiple Doses:
Initial LD: 50-400mg
Maint:
CrCl ≤50mL/min (No Dialysis): Give 50% of recommended dose
Regular Dialysis: Give 100% of recommended dose after each dialysis; on non-dialysis days, administer a reduced dose based on CrCl

ADMINISTRATION

Oral route

Take w/ or w/o food
Shake sus well before using

Sus
To reconstitute, add 24mL of distilled or purified water to bottle

HOW SUPPLIED

Sus: 10mg/mL, 40mg/mL [35mL]; Tab: 50mg, 100mg, 150mg, 200mg

CONTRAINDICATIONS

Coadministration with terfenadine (with multiple doses ≥400mg of fluconazole), other drugs known to prolong the QT interval and that are metabolized via the enzyme CYP3A4 (eg, cisapride, astemizole, erythromycin, pimozide, quinidine).

WARNINGS/PRECAUTIONS

Associated with rare cases of serious hepatic toxicity; monitor for more severe hepatic injury if abnormal LFTs develop. D/C if clinical signs and symptoms consistent with liver disease develop. Anaphylaxis reported (rare). Exfoliative skin disorders reported; closely monitor patients with deep seated fungal infections who develop rashes during treatment and d/c if lesions progress. D/C therapy if rash develops in patients treated for superficial fungal infection. QT prolongation and torsades de pointes reported (rare); caution with potentially proarrhythmic conditions. Caution in elderly or with renal/hepatic dysfunction. May impair mental/physical abilities. (Sus) Contains sucrose; do not use in patients with hereditary fructose, glucose/galactose malabsorption, and sucrase-isomaltase deficiency. (Tab) Consider risk versus benefits of single dose oral tab versus intravaginal agent therapy for the treatment of vaginal yeast infections.

ADVERSE REACTIONS

Headache, N/V, abdominal pain, diarrhea.

DRUG INTERACTIONS

See Contraindications. Carefully monitor coadministration of fluconazole at doses <400mg/day with terfenadine. Avoid with voriconazole. Risk of increased plasma concentration of compounds metabolized by CYP2C9 and CYP3A4; caution when coadministered and monitor patients carefully. May precipitate clinically significant hypoglycemia with oral hypoglycemics; monitor blood glucose and adjust dose of sulfonylurea as necessary. May increase PT with coumarin-type anticoagulants; monitor PT and, if necessary, adjust warfarin dose. May increase levels of phenytoin, cyclosporine, theophylline, rifabutin, oral tacrolimus, triazolam, celecoxib, halofantrine, flurbiprofen, racemic ibuprofen, methadone, saquinavir, sirolimus, and vinca alkaloids (eg, vincristine, vinblastine). May increase exposure of ethinyl estradiol and levonorgestrel. May reduce the metabolism and increase levels of tolbutamide, glyburide, and glipizide. Monitor SrCr with cyclosporine. Rifampin may enhance metabolism. May increase levels and psychomotor effects of oral midazolam; consider dose reduction of short-acting benzodiazepines metabolized by CYP450, and monitor appropriately. May increase systemic exposure to tofacitinib; reduce tofacitinib dose when given concomitantly. HCTZ may increase levels. May reduce clearance/distribution volume and prolong $T_{1/2}$ of alfentanil. May increase effect of amitriptyline and nortriptyline. May increase levels of zidovudine; consider dose reduction. May potentially increase systemic exposure of other NSAIDs that are metabolized by CYP2C9 (eg, naproxen, lornoxicam, meloxicam, diclofenac), and calcium channel antagonists. Risk of carbamazepine toxicity. May increase serum bilirubin and SrCr with cyclophosphamide. May significantly delay elimination of fentanyl, leading to respiratory depression. May increase risk of myopathy and rhabdomyolysis with HMG-CoA reductase inhibitors metabolized through CYP3A4 (eg, atorvastatin, simvastatin) or through CYP2C9 (eg, fluvastatin); monitor for symptoms and d/c statin if a marked increase in creatinine kinase is observed or myopathy/rhabdomyolysis is diagnosed or suspected. May inhibit the metabolism of losartan; monitor BP continuously. Acute adrenal cortex insufficiency reported after discontinuation of a 3-month therapy with fluconazole in a liver-transplanted patient treated with prednisone. CNS-related undesirable effects reported with all-trans-retinoid acid (an acid form of vitamin A).

PREGNANCY AND LACTATION

Category C (single 150mg tab use for vaginal candidiasis) and D (all other indications), caution in nursing.

MECHANISM OF ACTION

Triazole antifungal; selectively inhibits fungal CYP450 dependent enzyme lanosterol 14-α-demethylase, the enzyme that converts lanosterol to ergosterol. Subsequent loss of normal sterol correlates with the accumulation of 14-α-methyl sterols in fungi and may be responsible for the fungistatic activity.

PHARMACOKINETICS

Absorption: Rapid, almost complete. Absolute bioavailability (>90%); C_{max}=6.72mcg/mL (fasted, single 400mg dose); T_{max}=1-2 hrs (fasted). **Distribution:** Plasma protein binding (11-12%); found in breast milk. **Elimination:** Urine (80%, unchanged; 11%, metabolites); $T_{1/2}$=30 hrs (fasted). Refer to PI for pediatric and elderly pharmacokinetic parameters.

ASSESSMENT

Assess for hypersensitivity to the drug, renal/hepatic impairment, AIDS, malignancies, risk factors for QT prolongation, any other conditions where treatment is contraindicated or cautioned, pregnancy/nursing status, and possible drug interactions. Obtain specimens for fungal culture and other relevant lab studies (serology, histopathology) to isolate and identify causative organisms. (Sus) Assess for hereditary fructose, glucose/galactose malabsorption, and sucrase-isomaltase deficiency.

MONITORING

Monitor for signs/symptoms of liver disease, rash, and other adverse reactions. Monitor LFTs and renal function. Monitor PT when used with coumarin-type anticoagulants.

PATIENT COUNSELING

Inform about risks/benefits of therapy. Advise to notify physician if pregnant/nursing and counsel about potential hazard to the fetus if pregnant or pregnancy occurs. Instruct to inform physician of all medications currently being taken.

STORAGE

Tab: <30°C (86°F). Sus: Dry Powder: <30°C (86°F). Reconstituted: 5-30°C (41-86°F); discard unused portion after 2 weeks. Protect from freezing.

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