FLUCONAZOLE

http://www.aocd.org

Fluconazole is an antifungal medication used in the treatment of several fungal infections. The drug is used orally and intravenously. Fluconazole widely distributes into body tissues, nails and fluids including saliva, sputum, vaginal secretions. Fluconazole does not undergo first pass metabolism and is excreted mostly in the urine and some in the feces. This drug can also be used in the pediatric population.

Mechanism: Fluconazole works by altering the fungal cell membrane. It exerts its fungistatic effect by selectively inhibiting 14-alpha demethylase. This is a cytochrome P-450 enzyme that is necessary for synthesizing ergosterol, which is an important component of the fungal cell membrane. 14-alpha demethylase converts lanosterol to ergosterol. Without ergosterol, 14 alpha-methyl sterols increase which subsequently causes the fungal cell membrane to exhibit increased cellular permeability. This causes the components inside the cell to leak.

Uses: With its unique mechanisms of action, fluconazole has established a broad area of coverage in both dermatological and non-dermatological diseases. Fluconazole has good coverage against candida. Because it can penetrate the CSF, it can be used to treat cryptococcal meningitis. Other non-dermatological diseases it treats are esophageal candidiasis, bladder candidiasis, systemic candidiasis, fungal prophylaxis in bone marrow transplant, cystitis, urinary tract infections, and intra-abdominal infections. There are some additional off-label uses for fluconazole including treatment of blastomycosis, coccidiomycosis, and histoplasmosis.

Secondary to its mechanism of action, fluconazole finds utility in the following dermatologic diseases:

- Vulvovaginal candidiasis
- Oral candidiasis
- Mucocutaneous candidiasis

Side Effects: The drug is contraindicated in patients who are hypersensitive to azole antifungals and patients taking other QT prolonging medications. Fluconazole should be administered with caution in patients who have QT prolongation, proarrhythmic conditions like torsades de pointes, electrolyte abnormalities, renal impairment, heart disease, or preexisting hepatic disease. The drug should be dosed differently in patients who exhibit renal impairment. The most common adverse reaction is headache which occurs in greater than 10% of patients. Other adverse effects include nausea, rash, diarrhea, dyspepsia, taste changes, vomiting, abdominal pain and elevated liver transaminases. There are reports of fluconazole causing Stevens-Johnson syndrome and **toxic epidermal necrolysis**. Additionally, fluconazole can have an effect on phenytoin, cyclosporine, rifampin, and warfarin metabolism. Baseline renal function should be examined when first administering this drug and liver function should also be monitored. Treatment for various conditions with fluconazole during pregnancy is only recommended when the potential benefits outweigh the risks. There are reports of fluconazole causing birth defects when taken during the first trimester. The medication should be avoided in lactation due to a lack of literature available to assess its safety.

This information has been provided to you compliments of the American Osteopathic College of Dermatology and your physician.