OASIS DERMATOLOGY GROUP

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# Fluconazole

Fluconazole is a widely used antifungal agent belonging to the azole class of medications. It is available in both oral and intravenous formulations and is utilized for the treatment of various fungal infections. Due to its ability to distribute widely into body tissues, including nails, saliva, sputum, and vaginal secretions, fluconazole is effective for treating a range of systemic and superficial fungal infections. It is particularly valued for its ability to penetrate the blood-brain barrier, making it effective for central nervous system (CNS) infections like cryptococcal meningitis. Fluconazole is also used in pediatric populations, demonstrating its broad application across age groups.

**Pharmacokinetics**

Fluconazole is characterized by a favorable pharmacokinetic profile. The drug does not undergo first-pass metabolism and is excreted predominantly via the kidneys (approximately 80%) in its unchanged form, with a smaller amount excreted in the feces. This pharmacokinetic property makes fluconazole a reliable option for systemic infections. Its half-life of 30 hours allows for once-daily dosing, even in patients with normal renal function. In patients with renal impairment, the dosing regimen must be adjusted to account for decreased clearance.

**Mechanism of Action**

Fluconazole's primary mechanism of action is its inhibition of fungal cell membrane synthesis. It selectively inhibits 14-alpha demethylase, a cytochrome P450 enzyme that converts lanosterol to ergosterol, an essential component of the fungal cell membrane. This disruption leads to a reduction in ergosterol synthesis and accumulation of toxic 14-alpha-methyl sterols. The altered cell membrane becomes more permeable, resulting in the leakage of intracellular components, which disrupts the cell's function and leads to fungistatic effects. Although fluconazole is typically fungistatic, at higher concentrations, it may exhibit fungicidal properties.

**Therapeutic Uses**

Fluconazole is employed to treat a variety of fungal infections, both dermatological and non-dermatological:

- ***Candida Infections***: Fluconazole is particularly effective against Candida species, making it the drug of choice for vulvovaginal candidiasis, oral candidiasis, and mucocutaneous candidiasis. It is also used in the treatment of more systemic Candida infections, including esophageal candidiasis, bladder candidiasis, systemic candidiasis, and intra-abdominal infections.

- ***Cryptococcal Meningitis:*** Due to its ability to cross the blood-brain barrier, fluconazole is commonly used in the treatment and maintenance therapy for cryptococcal meningitis, especially in patients with HIV/AIDS.
- ***Fungal Prophylaxis:*** Fluconazole is used for prophylactic treatment in immunocompromised patients, particularly those undergoing bone marrow transplants, to prevent systemic fungal infections.
- ***Off-label Uses***: Fluconazole has demonstrated efficacy in treating blastomycosis, coccidiomycosis, and histoplasmosis, although these indications are considered off-label.

**Formulation and Dosing *****

**Adverse Effects and Drug Interactions**

Fluconazole is generally well-tolerated, but like all medications, it is associated with a variety of potential side effects:

- ***Common Side Effects***: These include headache, nausea, rash, diarrhea, dyspepsia, taste changes, vomiting, and abdominal pain. Elevated liver transaminases may also occur, necessitating monitoring of liver function during prolonged therapy.
- ***Serious Adverse Effects***: More severe reactions, although rare, include Stevens-Johnson syndrome and toxic epidermal necrolysis, both of which require immediate discontinuation of the drug.
- ***QT Prolongation***: Fluconazole can cause QT interval prolongation on an electrocardiogram, especially when used in conjunction with other QT-prolonging drugs. It should be used with caution in patients with preexisting cardiac conditions, electrolyte abnormalities, or proarrhythmic conditions, such as torsades de pointes.
- ***Renal and Hepatic Considerations***: Fluconazole should be used cautiously in patients with renal impairment, as the drug is primarily excreted via the kidneys. In such cases, the dose should be adjusted based on the degree of renal dysfunction. Similarly, patients with hepatic disease require close monitoring of liver function due to the potential for hepatotoxicity.
- ***Drug Interactions***: Fluconazole can interact with other medications, including phenytoin, cyclosporine, rifampin, and warfarin, by affecting their metabolism through inhibition of cytochrome P450 enzymes. Consequently, careful monitoring and dose adjustments may be necessary when fluconazole is co-administered with these drugs. Let your provider know if you take any of these medications as a dose adjustment or alternate medication may be necessary.

**Use in Pregnancy and Lactation**

Fluconazole is contraindicated in pregnancy for systemic infections, especially in the first trimester, due to reports of birth defects associated with high doses of fluconazole. The use of fluconazole during pregnancy should be limited to situations where the potential benefit

outweighs the risk. Fluconazole is also contraindicated during lactation due to the lack of sufficient safety data regarding its transfer into breast milk.

## Conclusion

Fluconazole remains a cornerstone in the treatment of fungal infections, particularly those caused by Candida and Cryptococcus species. Its broad spectrum of activity, ease of administration, and ability to penetrate deep tissues, including the CNS, make it an essential tool in clinical practice. However, clinicians must be vigilant about potential side effects, particularly those related to liver function, renal impairment, and QT prolongation. As with any medication, appropriate monitoring and consideration of drug interactions are crucial to ensuring optimal patient outcomes.

## References

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