Other Considerations
• Systemic azoles may have significant drug–drug interactions with ARV drugs (refer to Drug–Drug Interactions section of the Adult and Adolescent Antiretroviral Guidelines) and other drugs used for the treatment of opportunistic infections (refer to Table 4: Significant Pharmacokinetic Interactions Between Drugs Used to Treat or Prevent Opportunistic Infections). Consider TDM if prolonged use is indicated. • Fluconazole, itraconazole, posaconazole, and voriconazole can increase the risk for QTc prolongation, especially when co-administered with other QTc prolonging drugs that are cleared by CYP3A4. • Chronic or prolonged use of azoles might promote development of resistance.
Considerations During Pregnancy and Lactation
• Topical therapy is preferable for treatment of oral candidiasis and vulvovaginal candidiasis in pregnancy. Oral fluconazole should be avoided when treating vulvovaginal candidiasis in the first trimester (AIII). • During pregnancy, substitution of amphotericin B for fluconazole in the first trimester is recommended for invasive or refractory esophageal *Candida* infections (AIII). • Human data are not available for micafungin, anidulafungin, caspofungin, thus their use in human pregnancy is not recommended (AIII). Human data on the use of voriconazole are also not available, so its use is not recommended. • Oteseconazole is contraindicated during pregnancy and when lactating as animal studies have shown fetal malformations including ocular toxicity. Due to its long half-life, it is also contraindicated in females of reproductive potential despite the use of oral or other contraception. • Ibrexafungerp is teratogenic in animal studies. Use during pregnancy and when lactating is contraindicated.

Key: ARV = antiretroviral; CYP = cytochrome P450; IV = intravenous; PO = orally; QTc = QT corrected for heart rate; TDM = therapeutic drug monitoring

Oropharyngeal Candidiasis

Oral fluconazole is as effective as or superior to topical therapy for oropharyngeal candidiasis.[14] In addition, oral therapy is more convenient than topical therapy and usually better tolerated. Oral therapy has the additional benefit over topical regimens of being efficacious in treating esophageal candidiasis. Oral fluconazole at 100 to 200 mg once a day is considered the drug of choice to treat oropharyngeal candidiasis except during pregnancy **(AI).**[14] One to 2 weeks of therapy until resolution of infection is recommended for oropharyngeal candidiasis.[14]

Using topical agents to treat oropharyngeal candidiasis includes several advantages: it reduces systemic drug exposure, diminishes the risk of drug–drug interactions and systemic adverse events, and may reduce the likelihood that antifungal resistance develops. As an alternative to oral fluconazole, once-daily miconazole in 50-mg mucoadhesive buccal tablets **(BI)** or five-times-per-day clotrimazole troches can be used to treat oropharyngeal candidiasis **(BI);** these regimens were shown to be equivalent in a multicenter, randomized study. Nystatin suspension four times daily remains an additional alternative **(BII).**[15] Unfavorable taste and multiple daily dosing, such as in the cases of clotrimazole and nystatin, may lead to decreased tolerability of and adherence to these topical therapies. If esophageal involvement is suspected, topical therapy alone is not recommended **(AI).**

Itraconazole is formulated as an oral solution or capsules, which differ in dosing and efficacy. Oral itraconazole for 7 to 14 days is as effective as oral fluconazole for oropharyngeal candidiasis but less well tolerated.[16] Posaconazole oral suspension[17] is also as effective as fluconazole and generally better tolerated than itraconazole solution, but it is more expensive. Although both posaconazole and