

Rates of relapse are high in people with azole-refractory oropharyngeal or esophageal candidiasis who have initially responded to echinocandins, voriconazole, or posaconazole therapy. In such people, secondary prophylaxis should be instituted until immune reconstitution is achieved with the use of ART **(AIII)**.

For information regarding oteseconazole and ibrexafungerp, see the Vulvovaginal Candidiasis Treatment Section above.

When to Stop Suppressive Therapy

In situations where secondary prophylaxis has been instituted, no data exist to guide recommendations regarding its discontinuation. Based on experience with other opportunistic infections, it would be reasonable to discontinue secondary prophylaxis when the CD4 count has increased to >200 cells/mm³ following initiation of ART **(AIII)**.

Special Considerations During Pregnancy

Pregnancy increases the risk of vaginal colonization with *Candida* species. During pregnancy, diagnosis and management of oropharyngeal, esophageal, and vulvovaginal candidiasis are the same as for other people with HIV, with several considerations.

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)**. Data derived from women with vulvovaginal candidiasis suggest that fluconazole should not be used at any dose (including a single 150-mg dose) in the first trimester due to the risk of spontaneous abortion, while higher exposures (>150 mg dosing) during the first trimester are associated with cardiac septal closure defects.⁴⁶⁻⁵⁰ A recent analysis of registry data from Sweden and Denmark did not find any increase in stillbirth or neonatal death associated with exposure to fluconazole at any dose during pregnancy.⁵¹ Five cases of a syndrome consisting of craniosynostosis, characteristic facies, digital synostosis, and limb contractures (fluconazole embryopathy) have been reported in women chronically prescribed fluconazole at doses of 400 mg daily or higher in pregnancy.⁴⁸ A report from a national cohort register in Denmark found an increased hazard ratio (HR) of 1.48 for spontaneous pregnancy loss with any exposure to oral fluconazole from 7 to 22 weeks of pregnancy compared to unexposed, matched controls.⁴⁹ An increased HR of 1.47 was also noted with low-dose (150–300-mg cumulative dose) exposure. No increase in stillbirth was seen with fluconazole exposure broadly, but an increase in risk of stillbirth (HR, 4.10) was noted with fluconazole doses >300 mg.

Based on these data, substitution of amphotericin B for fluconazole in the first trimester is recommended for invasive or refractory esophageal *Candida* infections **(AIII)**. Neonates born to those receiving chronic amphotericin B at delivery should be evaluated for renal dysfunction and hypokalemia.

Other azoles are similarly not recommended in pregnancy. Itraconazole at high doses has been shown to be teratogenic in animals,⁵² but the metabolic mechanism accounting for these defects is not present in humans, so the data supporting this finding are of uncertain significance to human pregnancy. Case series in humans do not suggest an increased risk of birth defects with itraconazole,⁵³ but experience is limited. Human data are not available for posaconazole; however, the drug was associated with skeletal abnormalities in rats and was embryotoxic in rabbits when