

INDICATION	PRIMARY TREATMENT	PRECAUTIONS	SECONDARY TREATMENT	COMMENTS
Invasive disease ^b	Voriconazole, isavuconazole, posaconazole	Drug interactions (especially with rifampin and carbamazepine) ^c	AmB, caspofungin, posaconazole, micafungin	As primary therapy, voriconazole, isavuconazole, and posaconazole have a 20% higher response rate than AmB. Therapeutic drug monitoring is recommended for voriconazole.
Prophylaxis	Posaconazole tablet, itraconazole solution SUBA-itraconazole	Vincristine, cyclophosphamide interaction	Micafungin, aerosolized AmB	Some centers monitor plasma levels of itraconazole and posaconazole.
Single aspergilloma	Surgical resection	Multicavity disease: poor outcome of surgery, medical therapy preferable	Itraconazole, voriconazole, intracavity AmB	Single large cavities with an aspergilloma are best resected. Relapse reduced by pre- and peri-operative antifungal therapy.
Chronic pulmonary disease ^b	Voriconazole, itraconazole	Poor absorption of itraconazole capsules with proton pump inhibitors or H ₂ blockers	Posaconazole, IV AmB, IV micafungin	Resistance may emerge during treatment, especially if plasma drug levels are subtherapeutic. Resistance is less common with voriconazole.
ABPA/SAFS ("fungal asthma")	Itraconazole	Some glucocorticoid interactions, including with inhaled formulations	Voriconazole, posaconazole	Long-term therapy is helpful in most cases. No evidence indicates whether therapy modifies progression to bronchiectasis/fibrosis.

^aFor information on duration of therapy and drug resistance in certain *Aspergillus* species, see text. ^bAn infectious disease consultation is appropriate for these patients.

^cOnline drug-interaction resource: www.aspergillus.org.uk/content/antifungal-drug-interactions.

Note: After loading doses, the oral dose is usually 200 mg bid for voriconazole and itraconazole, 100 mg bid for SUBA-itraconazole, 300 mg qd for posaconazole tablets, and 200 mg qd for isavuconazole. The IV dose of voriconazole for adults is 6 mg/kg twice at 12-h intervals (loading doses) followed by 4 mg/kg q12h; a larger dose is required for children and teenagers; a lower dose may be safer for persons >70 years of age. Plasma monitoring is helpful in optimizing the dosage. The IV dose of isavuconazole is 200 mg tid for 2 days (loading dose) followed by 200 mg qd. Caspofungin is given as a single loading dose of 70 mg and then at 50 mg/d; some authorities use 70 mg/d for patients weighing >80 kg, and lower doses are required with hepatic dysfunction. Micafungin is given as 50 mg/d for prophylaxis and as at least 150 mg/d for treatment; this drug has not yet been approved by the U.S. Food and Drug Administration (FDA) for this indication. AmB deoxycholate is given at a daily dose of 1 mg/kg if tolerated. Several strategies are available for minimizing renal dysfunction. Lipid-associated AmB is given at 3 mg/kg (AmBisome) or 5 mg/kg (Abelcet). Different regimens are available for aerosolized AmB, but none is FDA approved. Other considerations that may alter dose selection or route include age; concomitant medications; renal, hepatic, or intestinal dysfunction; and drug tolerability.

Abbreviations: ABPA, allergic bronchopulmonary aspergillosis; AmB, amphotericin B; SAFS, severe asthma with fungal sensitization.

Voriconazole, isavuconazole and posaconazole are the preferred agents for invasive aspergillosis; caspofungin, micafungin, and lipid-associated AmB are second-line agents. AmB is not active against *A. terreus* or *A. nidulans*; multi-azole resistance in *A. fumigatus* is present in <5% of isolates but is increasing, especially in Southeast Asia; and *A. niger* is resistant to itraconazole and isavuconazole. An infectious disease consultation is advised for patients with invasive disease, given the complexity of management. Immune reconstitution can complicate recovery. The duration of therapy for invasive aspergillosis varies from ~3 months to several years, depending on the patient's immune status and response to therapy. Relapse occurs if the response is suboptimal and immune reconstitution is not complete.

Voriconazole is currently the preferred oral agent for chronic aspergillosis with itraconazole or posaconazole as substitutes when failure, emergence of resistance, or adverse events occur. Because chronic cavitary pulmonary aspergillosis responds slowly, therapy for >6 months is necessary, and disease control may require years of treatment, whereas the duration of treatment for other forms of chronic and allergic aspergillosis requires case-by-case evaluation. Glucocorticoids should be used in chronic cavitary pulmonary aspergillosis only if covered by adequate antifungal therapy. Acute