

# MEDICAL THERAPY

**Table 1. Selected antifungal agents with activity against *Aspergillus*.**

Drug class, drug name (brand/investigational name)	Formulation
Polyene	
Amphotericin B deoxycholate (Fungizone) <sup>a</sup>	Intravenous
Amphotericin B lipid complex (Abelcet) <sup>a</sup>	Intravenous
Amphotericin B colloidal dispersion (Amphocil; Amphotec) <sup>a</sup>	Intravenous
Liposomal amphotericin B (AmBisome) <sup>a</sup>	Intravenous
Liposomal nystatin (Nyotran)	Intravenous
Triazole	
Itraconazole (Sporanox) <sup>a</sup>	Oral, intravenous
Voriconazole (Vfend) <sup>a</sup>	Oral, intravenous
Posaconazole (SCH 56592)	Oral
Ravuconazole (BMS-207147; ER-30346)	Oral
Echinocandin	
Caspofungin (Cancidas) <sup>a</sup>	Intravenous
Anidulafungin (VER-002; LY303366)	Intravenous
Micafungin (FK463)	Intravenous

<sup>a</sup> Licensed for clinical use in United States.

Table 2. – Medical therapy in invasive pulmonary aspergillosis

Medical therapy	Dosage	Response %	Comments
Amphotericine B Desoxycholate	1–1.5 mg·kg <sup>-1</sup>	33–54	Mortality of 64–90% Fewer side effects in continuous 24 h infusion Local instillation possible Not effective in prophylaxis
Colloid dispersion	3–4 mg·kg <sup>-1</sup>	38–48	Less nephrotoxicity, but severe side-effects as fever, chills, hypoxia
Lipid complex	4.8 mg·kg <sup>-1</sup>	42–67	Less nephrotoxicity, but chills, rigor, fever
Liposomal	1–3 (-6) mg·kg <sup>-1</sup>	30–60	Less nephrotoxicity Less breakthrough infections Reduced aspergillus colonization
Azoles			
Itraconazole	Oral 400–600 mg	39–66	Side effects: nausea and vomiting Better resorption as oral solution
Voriconazole	<i>i.v.</i> 200 mg	48 50–75	Long term therapy induces resistance Visual, hepatic, and dermal side effects FDA approval pending
Posaconazole		53	FDA approval pending
Racuvonazole			Only animal studies
Echinocandins			
Caspofungin (MK-0991)		41–45	Preliminary data from clinical trials
FK 463			In clinical trials
LY-303366			In clinical trials
Papulacandins			In development
Acidic terpenoids			In development

FDA: Food and Drug Administration.

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**Table 2. Summary of recommendations for the treatment of aspergillosis.**

Condition	Therapy <sup>a</sup>		Comments
	Primary	Alternative <sup>b</sup>	
Invasive pulmonary aspergillosis	Voriconazole (6 mg/kg IV every 12 h for 1 day, followed by 4 mg/kg IV every 12 h; oral dosage is 200 mg every 12 h)	L-AMB (3–5 mg/kg/day IV), ABLC (5 mg/kg/day IV), caspofungin (70 mg day 1 IV and 50 mg/day IV thereafter), micafungin (IV 100–150 mg/day; dose not established <sup>c</sup> ), posaconazole (200 mg QID initially, then 400 mg BID PO after stabilization of disease <sup>d</sup> ), itraconazole (dosage depends upon formulation) <sup>e</sup>	Primary combination therapy is not routinely recommended based on lack of clinical data; addition of another agent or switch to another drug class for salvage therapy may be considered in individual patients; dosage in pediatric patients for voriconazole is 5–7 mg/kg IV every 12 h and for caspofungin is 50 mg/m <sup>2</sup> /day; limited clinical experience is reported with anidulafungin; dosage of posaconazole in pediatric patients has not been defined; indications for surgical intervention are outlined in table 3
Invasive sinus aspergillosis	Similar to invasive pulmonary aspergillosis	Similar to invasive pulmonary aspergillosis	Similar to invasive pulmonary aspergillosis
Tracheobronchial aspergillosis	Similar to invasive pulmonary aspergillosis	Similar to invasive pulmonary aspergillosis	Similar to invasive pulmonary aspergillosis

Chronic necrotizing pulmonary aspergillosis (subacute invasive pulmonary aspergillosis)	Similar to invasive pulmonary aspergillosis	Similar to invasive pulmonary aspergillosis	Because chronic necrotizing pulmonary aspergillosis requires a protracted course of therapy measured in months, an orally administered triazole, such as voriconazole or itraconazole, would be preferred over a parenterally administered agent
Aspergillosis of the CNS	Similar to invasive pulmonary aspergillosis	Similar to invasive pulmonary aspergillosis	This infection is associated with the highest mortality among all of the different patterns of invasive aspergillosis; drug interactions with anticonvulsant therapy
<i>Aspergillus</i> infections of the heart (endocarditis, pericarditis, and myocarditis)	... <sup>f</sup>	Similar to invasive pulmonary aspergillosis	Endocardial lesions caused by <i>Aspergillus</i> species require surgical resection; aspergillus pericarditis usually requires pericardiectomy
<i>Aspergillus</i> osteomyelitis and septic arthritis	... <sup>f</sup>	Similar to invasive pulmonary aspergillosis	Surgical resection of devitalized bone and cartilage is important for curative intent
<i>Aspergillus</i> infections of the eye (endophthalmitis and keratitis)	Intraocular AMB indicated with partial vitrectomy <sup>f</sup>	Similar to invasive pulmonary aspergillosis; limited data with echinocandins	Systemic therapy may be beneficial in management of aspergillus endophthalmitis; ophthalmologic intervention and management is recommended for all forms of ocular infection; topical therapy for keratitis is indicated

Cutaneous aspergillosis	...	Similar to invasive pulmonary aspergillosis	Surgical resection is indicated where feasible
<i>Aspergillus</i> peritonitis	...	Similar to invasive pulmonary aspergillosis	...
Empirical and preemptive antifungal therapy	For empirical antifungal therapy, L-AMB (3 mg/kg/day IV), caspofungin (70 mg day 1 IV and 50 mg/day IV thereafter), itraconazole (200 mg every day IV or 200 mg BID), voriconazole (6 mg/kg IV every 12h for 1 day, followed by 3 mg/kg IV every 12 h; oral dosage is 200 mg every 12 h)	...	Preemptive therapy is a logical extension of empirical antifungal therapy in defining a high-risk population with evidence of invasive fungal infection (e.g., pulmonary infiltrate or positive galactomannan assay result)
Prophylaxis against invasive aspergillosis	Posaconazole (200 mg every 8h)	itraconazole (200 mg every 12 h IV for 2 days, then 200 mg every 24 h IV) or itraconazole (200 mg PO every 12 h); micafungin (50 mg/day)	Efficacy of posaconazole prophylaxis demonstrated in high-risk patients (patients with GVHD and neutropenic patients with AML and MDS)
Aspergilloma <sup>a</sup>	No therapy or surgical resection	itraconazole or voriconazole; similar to invasive pulmonary aspergillosis	The role of medical therapy in treatment of aspergilloma is uncertain; penetration into preexisting cavities may be minimal for AMB but is excellent for itraconazole
Chronic cavitary pulmonary aspergillosis <sup>a</sup>	Itraconazole or voriconazole	Similar to invasive pulmonary aspergillosis	Innate immune defects demonstrated in most of these patients; long-term therapy may be needed; surgical resection may lead to significant complications; anecdotal responses to IFN- $\gamma$
Allergic bronchopulmonary aspergillosis	Itraconazole	Oral voriconazole (200 mg PO every 12 h) or posaconazole (400 mg PO BID)	Corticosteroids are a cornerstone of therapy; itraconazole has a demonstrable corticosteroid-sparing effect
Allergic aspergillus sinusitis	None or itraconazole	Few data on other agents	