Antifungal Drugs Table

Drug Class & Drugs	Mechanism of Action	Pharmacokinetics (PK) & Resistance	Clinical Uses	Adverse Effects (AEs) & Contraindications
Polyene Macrolides -Amphotericin B -Nystatin	-Binds **ergosterol** of fungal cell membrane, forming pores that allow leakage of intracellular ions →cell death	**PK:** -Ampho B: Poor PO absorption; given as **slow IV infusion** (complexed with deoxycholate or **liposomal** to reduce toxicity) -Highly protein bound, poor BBB penetration **Resistance:** Modifying the sterol target	-**Ampho B:** Broad spectrum & fungicidal (Candida, Cryptococcus, endemic mycosis, **Aspergillus**) -**Nystatin:** Only used **topically** (skin, mucous membranes) due to high toxicity.	**-Infusion-related toxicity:** Fever, chills, vomiting, hypotension (**reduced by slowing infusion rate**) **-Nephrotoxicity:** Common (>80%) and most serious (has reversible and irreversible components) -Anemia (reduced erythropoietin)
Pyrimidine Analog -Flucytosine	-Converted intracellularly to 5-fluorouracil → **inhibits DNA and RNA synthesis** **-** Enters fungal cell via **Cytosine permease**	**-PK:** Given PO & IV. Widely distributed including **CNS** **-Resistance: Emerges rapidly during monotherapy**	-Narrow spectrum (yeasts) -**Synergistic effect with Amphotericin B** for cryptococcal meningitis	-Narrow therapeutic window -GIT disturbances -**Bone marrow depression** (anemia, neutropenia, thrombocytopenia)

Azoles **-*Imidazoles*:** Ketoconazole, Miconazole, Clotrimazole **-*Triazoles*:** Fluconazole, Itraconazole, Voriconazole	-**Inhibition of fungal cytochrome P450** responsible for synthesis of **ergosterol** → altered membrane fluidity	**-Fluconazole:** High PO availability, reaches **high concentration in CSF**, **excreted unchanged in urine → excellent for fungal UTIs** -**Itraconazole:** Extensive first-pass, absorption increased by low gastric pH -**Voriconazole:** Eliminated by hepatic metabolism	-**Fluconazole: Drug of choice for most fungal meningitis** and candidemia. (No activity against Aspergillus) -**Itraconazole: Drug of choice for dimorphic fungi** (Histoplasma, Blastomyces) -**Voriconazole: Invasive aspergillosis** -**Topicals:** Vulvovaginal candidiasis, oral thrush, tinea	-Imidazoles inhibit human P450 → **high incidence of drug interactions** - **Fluconazole:** Widest therapeutic index, hepatitis -**Itraconazole:** Interacts with P450s, hepatitis, hypokalemia -**Voriconazole: Transient visual disturbances** (color vision/brightness)
Allylamines -Terbinafine	-Inhibits **squalene epoxidase** → toxic accumulation of squalene in fungal cell	**-PK:** -Given PO & topically **-Highly lipophilic and keratinophilic** (taken up by skin, nails)	**-Fungal infections of the nails (onychomycosis)** -Topically for tinea cruris/corporis	-GIT disturbances -Joint and Muscle pain -Headache, dizziness -Hepatitis

Echinocandins -Caspofungin -Micafungin -Anidulafungin	• Inhibit synthesis of **B(1,3)-glucan** (necessary for fungal cell wall structure) → cell lysis → death	**PK:** -Available **only IV** (poor PO absorption) -Water soluble, highly protein bound	Candidiasis(mucocutaneous, septicemia, esophageal) **-Empiric therapy in febrile neutropenia** -**Salvage therapy for invasive aspergillosis**	-Generally **well tolerated** -**Anidulafungin releases histamine** (flushing, rash) -Micafungin increases levels of some immunosuppressants