Systemic antifungal agents for superficial and deep infections: select pharmacokinetic parameters and approved indications

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| Drug classes and names (administration route)  Mode of action for class | Central nervous system penetration | Urinary excretion\* | Approved indications**†** |
| Azoles: Inhibit the cytochrome P450-dependent synthesis of ergosterol, a key component of the fungal cell membrane, via action on lanosterol 14-α-demethylase | | | |
| Fluconazole (oral and intravenous) 1,2 | High 3 | 80% of dose in active form | * *Candida:* mucosal (oropharyngeal, oesophageal, urogenital), chronic mucocutaneous, cutaneous, and invasive infections. Onychomycosis only when when other agents are not considered appropriate * *Malassezia*: skin infections * *Cryptococcus:* meningitis * Dermatophytes: skin infections, and onychomycosis (see *Candida* onychomycosis) * *Coccidioides:* infections |
| Isavuconazole (oral and intravenous) 2,4 | High (but low penetration into the CSF)3 | Less than 1% of dose in active form 3 | * *Aspergillus*: invasive infections * *Mucorales:* invasive infections |
| Itraconazole  (oral) 2 | Low 3 | Less than 1% of dose in active form | * *Candida:* oropharyngeal, vulvovaginal and nail infections. Invasive infections when first-line therapy is ineffective or inappropriate * *Cryptococcus:* Invasive infections when first-line therapy is ineffective or inappropriate * *Malassezia:* pityriasis versicolor * *Aspergillus:* pulmonary and extrapulmonary infections in patients who are intolerant of or refractory to amphotericin B therapy * Dermatophytes: skin and nail infections * *Blastomyces:* pulmonary and extrapulmonary infections * *Histoplasma*: pulmonary and disseminated, non-meningeal infections |
| Posaconazole (oral) 2,4 | Low 3 | Less than 1% of dose in active form | * *Candida:* oropharyngeal infection in patients who do not respond to itraconazole or fluconazole * *Aspergillus:* invasive infections in patients who do not respond to or are intolerant of amphotericin B or itraconazole * *Fusarium:* infections in patients who do not respond to or are intolerant of amphotericin B * Dematiaceous fungi: chromoblastomycosis and mycetoma in patients who do not respond to or are intolerant to itraconazole * *Coccidioides:* Infection in patients who do not respond to or are intolerant of amphotericin B, itraconazole or fluconazole |
| Voriconazole (oral and intravenous) 2,4 | High 3 | Less than 2% of dose in active form | * *Candida*: esophageal infection. Candidemia in non-neutropenic patients. Fluconazole-resistant serious invasive infections (including *C. krusei*) * *Aspergillus*: invasive infections * *Fusarium:* serious infections (including *F. solani*) * *Scedosporium*: serious infections |
| Echinocandins: Inhibit the formation of 1,3--D-glucan, an essential component of the fungal cell wall | | | |
| Anidulafungin  (*intravenous) 2,5* | Low 6 | Less than 1% of dose in active form | * *Candida*: esophageal infection. Candidemia, intra-abdominal abscess and peritonitis |
| Caspofungin  (intravenous) 2,4 | Low 6 | Less than 2% of dose in active form | * *Aspergillus*: invasive infections in patients who are refractory to or intolerant of amphotericin B, lipid formulations of amphotericin B or itraconazole. * *Candida:* esophageal infection, candidemia, invasive infections, intra-abdominal abscesses, peritonitis and pleural space infections |
| Micafungin  (intravenous)  2,4,7 | Low 6 | Less than 1% of dose in active form | * *Candida*: esophageal infection, candidemia, acute disseminated infections, peritonitis and abscesses |
| Halopyrimidine: Intracellular conversion to 5-fluorouracil which inhibits protein and DNA synthesis | | | |
| Flucytosine (oral and intravenous) 2 | High | Main excretion route of active form | * *Candida* and *Cryptococcus:* serious infections caused by susceptible strains |
| Polyene: Binds to ergosterol in the fungal cell membrane | | | |
| Amphotericin B (intravenous) 2,8 | Low 9 | 2-5% of dose in active form and percentage increases over time | * Invasive infections due to: *Candida, Cryptococcus, Aspergillus, Absidia, Mucor, Rhizopus, Conidiobolus, Basidiobolus, Blastomyces, Coccidioides, Histoplasma, Sporothrix* * High dosages may be needed for mucormycoses 9 and clinical failures in infections caused by the *Entomophthorales* 10 |

\* Despite poor urinary excretion, therapeutic success has been reported for amphotericin B and micafungin in cases of *Candida* urinary tract infections 9,11

**†** Indications that have been approved for adults by the European Medicines Agency (EMEA, EMA,) and the U. S. Food and Drug Administration (FDA). Indications for individual drugs may differ between these agencies. Itraconazole and amphotericin B were approved by national medicine agencies before the establishment of EMEA (which became EMA) and information from the British electronic Medicines Compendium (eMC) is used, as an example, for these drugs. Approved indications for the use of antifungals in children and for empirical and prophylactic therapy are not displayed.

References

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