

## LIPID-BASED ANTIFUNGAL AGENTS

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The spectrum of human mycoses ranges from superficial and local to disseminated and life-threatening infections. Opportunistic fungal infections of the immunocompromised host are difficult to treat and result in significant mortality. Antifungal drugs with a broad spectrum of activity along with acceptable efficacy and an optimal safety profile are an option for the treatment of these infections. Amphotericin B deoxycholate, which is the cornerstone of parenteral antifungal therapy, is effective against most common invasive fungal infections. However, its toxicity is frequently beyond acceptable limits. Studies to develop amphotericin B varieties that are less toxic and at least as effective as the parent compound have successfully resulted in the emergence of three lipid varieties of amphotericin B. These are amphotericin B lipid complex (ABLC; Abelcet<sup>®</sup>, Elan Pharmaceu.), amphotericin B colloidal dispersion (ABCD; Amphocil<sup>®</sup> or Amphotec<sup>®</sup>, Sequus Pharmaceu.), and liposomal amphotericin B (L-AMB; Ambisome<sup>®</sup>, Nexstar Pharmaceu.). They were approved in the 1990s and are in clinical use [1, 2]. Their *in vitro* antifungal activity and range of *in vivo* efficacy are similar to that of amphotericin B deoxycholate. They are effective in the treatment of systemic candidiasis, invasive aspergillosis, cryptococcosis, zygomycosis, fusariosis, endemic (true systemic) mycosis, leishmaniasis, and febrile neutropenia refractory to antibacterial therapy. They may even occasionally provide enhanced *in vivo* efficacy, presumably due to their high concentrations in the reticuloendothelial system and enhanced delivery to the site of infection. Significantly, they are not licensed for first-line therapy in any of these fungal infections and indicated for use only in case of the failure or toxicity of amphotericin B deoxycholate. Their most striking advantage is their significantly reduced nephrotoxicity and enhanced safety compared to amphotericin B deoxycholate. The infusion-related side effects due to these varieties are also less common than for the parent compound, but they tend to differ from one variety to another. Lipid-based amphotericin B varieties can safely be used at doses as high as 3-7 mg/kg. While these advantages make them very attractive, their high cost remains a major drawback [1-4]. The liposomal variety of nystatin (Nyotran<sup>®</sup>, Aronex Pharmaceu.) is another lipid-based antifungal drug which is currently undergoing late Phase III clinical trials. It appears to have enabled the systemic use of nystatin without toxicity. Liposomal nystatin appears to be effective in the treatment of candidiasis, aspergillosis and febrile neutropenia that have proved unresponsive to antibacterial therapy. If it is

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approved in the future, liposomal nystatin may be a second- or third-line salvage agent, particularly in candidiasis and aspergillosis unresponsive to currently available antifungal drugs [5].

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