Micafungin in a nutshell: state of affairs on the pharmacological and clinical aspects of the novel echinocandin

Micafungin is one of three echinocandin antifungals approved by the US FDA and the European Medicines Agency (EMA). Like all echinocandin antifungals, micafungin inhibits the synthesis of 1,3-β-D-glucan, a main component of the cell wall of many medically important fungi; thus, exerting fungicidal activity against most Candida spp., as well as fungistic activity against many Aspergillus spp. Micafungin displays linear pharmacokinetics over the therapeutic range with a long half-life, allowing once-daily intravenous administration. Steady state serum concentrations are achieved after 3 days. Since therapeutic concentrations of micafungin are achieved after the administration of a standard dose there is no need for a loading dose. Interactions of micafungin with the cytochrome P450 (CYP3A4) system are marginal; and, consequently, no severe drug–drug interactions have been reported so far. Furthermore, micafungin exhibited favorable profiles for tolerability and safety; no dose-limiting toxicity has been established yet. However, despite its favorable characteristics, there are no unique features among the echinocandins. Nevertheless, micafungin is the only echinocandin that has been approved for the prophylaxis of Candida spp. infections in patients undergoing hematopoietic stem cell transplantation.

KEYWORDS: antifungal agents, aspergillosis, candidiasis, dose–response relationship, drug administration schedule, drug interactions, lipopeptides

The incidence of invasive fungal diseases (IFDs) has increased, mainly owing to the growing number of immunocompromised patients in recent years. The most common pathogens of IFDs in the immunocompromised host are Candida spp. and Aspergillus spp. Infections caused by Candida spp. account for 8–10% of all nosocomial bloodstream infections in US hospitals [1]. Despite new antifungal therapies, the attributable mortality rate of up to 49% remains unacceptably high [2]. The emergence of infections caused by Candida spp. other than Candida albicans has been repeatedly reported [1,3].

Aspergillus spp. are ubiquitous soil-dwelling fungi that may cause life-threatening IFD in immunocompromised patients. The most common (80–90%) form of invasive aspergillosis (IA) is invasive pulmonary aspergillosis.

Echinocandin class

Echinocandin antifungals are a recent addition to the antifungal armamentarium. They target the fungal cell wall by inhibiting the production of 1,3-β-D-glucan. Currently, three antifungals of the echinocandin class are commercially available. The first echinocandin to gain approval from the US FDA was caspofungin. Approval was granted for the following indications: empirical treatment of presumed fungal infections in patients with febrile neutropenia (FN), treatment of esophageal candidiasis, candidemia and other Candida spp. infections, as well as the treatment of IA in patients who are refractory or intolerant to other therapies [101]. Micafungin has been approved by the European Medicines Agency (EMA) in April 2008 and the FDA in March 2005 for the treatment of patients with esophageal candidiasis, invasive candidiasis and the prophylaxis of Candida infections in patients undergoing hematopoietic stem cell transplantation (HSCT) [101,102]. Anidulafungin is the latest antifungal agent of this class and has been approved by the FDA for the treatment of esophageal candidiasis, candidemia and other Candida spp. infections [103]. The EMA approved anidulafungin for the treatment of invasive candidiasis in adult non-neutropenic patients [104].

Micafungin

Micafungin is derived from the water-soluble echinocandin-like fermentation product (lipopeptide FR901379) of Coleophoma empetri F-11889, by replacement of the lipophilic side chain, which results in a reduced hemolytic potential [101].

The chemical designation of micafungin sodium is pneumocandin A0, 1-[(4R,5R)-4,5-dihydroxy-N2-[4-[(5’-4’-(pentyloxy)
Micafungin acts as a noncompetitive inhibitor of 1,3-β-D-glucan synthesis; hence, inhibiting the production of a main component of the cell wall in many medically important fungi. Consequently, the fungal cell walls become less stable and unable to resist osmotic pressure, which ultimately leads to cell lysis. It has been demonstrated that even low concentrations of micafungin result in a marked effect on the cell wall, in other words, morphological changes and occasional cell lysis, of Candida albicans [4,5]. The in vitro activity of micafungin was determined against 5346 invasive (bloodstream or sterile site) isolates of Candida spp. collected from over 90 medical centers worldwide. Micafungin demonstrated high activity against Candida spp. with minimal inhibitory concentrations (MIC) of 0.015 µg/ml for 50% (MIC50) and 1 µg/ml for 90% (MIC90) of all tested isolates (Table 1). Micafungin at doses of 2 µg/ml or less successfully inhibited all isolates. The least micafungin-susceptible strains, with MIC90 ranging from 1 to 2 µg/ml, were Candida parapsilosis, Candida guilliermondii and Candida famata. In an in vitro time-to-kill study, micafungin did not exhibit fungicidal activity against C. parapsilosis [6]. In vivo, however, the treatment response rate of micafungin against C. parapsilosis was comparable to those against other Candida spp. [7]. No significant changes in the activity against strains of Candida were noticed during the 6-year study period from January 2001 to December 2006 [8]. Resistance to micafungin may be caused by mutations within highly conserved regions of the FSK1, and, to a lesser extent, FSK2 genes, which encode for certain subunits of the 1,3-β-D-glucan synthase [9]. However, recent results from a large and geographically diverse Candida spp. collection (n = 133) demonstrated that mutations of the FSK1 gene remain uncommon among isolates with various MIC levels [10].

Micafungin also demonstrated good in vitro antifungal activity against clinical isolates of Aspergillus flavus (n = 18), Aspergillus fumigatus (n = 35), Aspergillus nidulans (n = 3), Aspergillus niger (n = 20), Aspergillus terreus (n = 12) and Aspergillus versicolor (n = 3). However, minimum effective concentrations were not reported [11-13]. In an experimental model of guinea pigs suffering from invasive pulmonary aspergillosis, micafungin was markedly less effective than voriconazole or amphotericin B [14]. In another model, micafungin failed to eliminate invasive pulmonary aspergillosis caused by a clinical isolate of A. fumigatus in 27 neutropenic rabbits [15]. However, in the treatment of an experimental murine CNS aspergillosis, micafungin was more efficacious than voriconazole, caspofungin and conventional liposomal amphotericin B [16].

The in vitro activity of micafungin on dimorphic fungi considerably depends on their growth form. Micafungin demonstrated good activity against mycelial forms of Histoplasma capsulatum, Blastomyces dermatitidis and Coccioidioides immitis (MIC range 0.0078–0.0625 µg/ml), as well as some activity against mycelial forms of Sporothrix schenckii (MIC ≤ 1 µg/ml) and Penicillium marneffei (MIC ≤ 2 µg/ml). However, against the yeast-like forms of these fungi and both forms of Paracoccidioides brasilienis, the activity of micafungin was weak (MIC range from 4 to >64 µg/ml) [17]. The reported MIC of micafungin against zygomycetes was greater than 8 µg/ml [11,13]. Micafungin does not posses in vitro activity against important basidiomycetes, such as Cryptococcus spp., Rhodotorula spp. and Trichosporon spp. [12,13].

**Pharmacodynamics, pharmacokinetics & metabolism**

Micafungin is like all echinocandins, only available for intravenous administration. It exhibits a linear relationship between dose and area under the plasma concentration–time curve (AUC)
Thus, dose adjustments are not required in the body weight of the subjects and controls; this finding may have been caused by differences in the body weight of the subjects and controls. AUC and Cmax were approximately proportional evaluated in a dose-escalation study. On day 1, AUC and Cmax were approximately proportional to the administered dose, ranging from 12.5 to 200 mg. The mean terminal half-life time of approximately 13 h remained consistent following repeated and increasing doses of micafungin. The maximum tolerated dose, however, was not reached in this study [18].

Although Cmax and AUC were approximately 22% lower in patients with moderate hepatic dysfunction (Child–Pugh score of 7–9; n = 8), this finding may have been caused by differences in the body weight of the subjects and controls; thus, dose adjustments are not required [19].

Furthermore, no difference in the pharmacokinetics of micafungin caused by severe renal impairment (creatinine clearance <30 ml/min; n = 9) was observed [19], and since micafungin is highly protein bound (>99%), primarily to albumin, no additional dosing is necessary after hemodialysis [105].

In an open-label dose-escalation study in pediatric patients with FN (n = 77) the pharmacokinetic profile showed a linear relationship with the administered doses ranging from 0.5 to 4.0 mg/kg. The exhibited overall pharmacokinetic profile was similar to that observed in adults. However, the clearance in patients aged 2–8 years was increased approximately 1.35-fold compared with that of patients aged 9 years and older [20].

In a similar sequential-dose trial involving premature neonates (n = 23) the pharmacokinetic profile also appeared to be linear; although the terminal half-life was shorter (8 vs 13 h) and an even more rapid clearance of micafungin was observed compared with that in children and adults [21]. Recently, the population pharmacokinetics of micafungin in neonates and young infants from three clinical trials have been published. The analysis used data from 47 infants with a proven or presumptive diagnosis of disseminated candidiasis, who received micafungin at 0.75–15.00 mg/kg. The pharmacokinetics of micafungin were linear. The weight-normalized estimates of clearance and volume distribution approximated those previously described for adults [22].

The bronchopulmonary disposition of micafungin was observed in a recently published study of 15 healthy volunteers [23]. Following three 150 mg doses of micafungin daily, a bronchial alveolar lavage was performed at either 4, 12 or 24 h after the last dose. It was demonstrated that micafungin predominantly concentrates within alveolar macrophages with complete (106%) penetration relative to the total drug plasma exposure, achieving steady-state concentrations above the minimum effective concentration for germinated A. fumigatus [28]. In a comparable study, the intrapulmonary pharmacokinetics and pharmacodynamics of micafungin in adult lung transplant patients were investigated. In contrast to the study with healthy volunteers, only one dose (instead of three doses) of micafungin was administered prior to the pharmacokinetic sampling; hence, the AUC in plasma was lower, but the AUCs within the epithelial lining fluid and alveolar cells were similar [24].

Micafungin is metabolized by acylsulfatase (to the catechol form, M1) with secondary metabolism by catechol-O-methyltransferase (to the methoxy form, M2). Another metabolite (M5) is formed by hydroxylation of the side chain catalyzed by cytochrome P450 (CYP3A4) isozymes; although hydroxylation by CYP3A4 is not a major pathway for micafungin metabolism. None of these metabolites exhibit antifungal activity [105].

The elimination of micafungin has been studied by tracing 14C micafungin in radioactivity assays from urine and feces of healthy volunteers after the administration of a single radio-labeled dose (25 mg). The fecal radioactivity accounted for 71% of the administered dose, while the urine contained only trace amounts of unchanged micafungin [105].

### Table 1. In vitro susceptibilities of 5346 clinical isolates of Candida spp. to micafungin.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number of isolates</th>
<th>MIC90 [µg/ml]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candida albicans</td>
<td>2869</td>
<td>0.030</td>
</tr>
<tr>
<td>Candida parapsilosis</td>
<td>759</td>
<td>2.000</td>
</tr>
<tr>
<td>Candida glabrata</td>
<td>747</td>
<td>0.015</td>
</tr>
<tr>
<td>Candida tropicalis</td>
<td>625</td>
<td>0.060</td>
</tr>
<tr>
<td>Candida krusei</td>
<td>136</td>
<td>0.120</td>
</tr>
<tr>
<td>Candida guilliermondii</td>
<td>61</td>
<td>1.000</td>
</tr>
<tr>
<td>Candida lusitaniae</td>
<td>58</td>
<td>0.250</td>
</tr>
<tr>
<td>Candida kefyr</td>
<td>37</td>
<td>0.060</td>
</tr>
<tr>
<td>Candida famata</td>
<td>24</td>
<td>1.000</td>
</tr>
<tr>
<td>Candida spp.</td>
<td>30</td>
<td>0.500</td>
</tr>
<tr>
<td>Total</td>
<td>5346</td>
<td>1.000</td>
</tr>
</tbody>
</table>

MIC90: Minimal inhibitory concentration at which at least 90% of isolates are inhibited. Adapted from [6].
Pharmacokinetic in vitro data suggest that micafungin is unlikely to cause drug–drug interactions by inhibition of CYP3A4 and the multidrug resistance protein-1 [25]. However, micafungin does alter the pharmacokinetics of sirolimus, nifedipine and itraconazole, increasing the AUC of these substances by 21, 18 and 22%, respectively [105]. Therefore, these levels should be monitored. The clearance of cyclosporine is decreased by 10% during concomitant administration of micafungin [26].

Coadministration of micafungin does not significantly affect the plasma levels of tacrolimus [27,28], voriconazole [29], fluconazole [105], amphotericin B deoxycholate [30], mycophenolate mofetil [105] and prednisolone [105].

Concomitant therapy with rifampin [31,105], ritonavir [31,105], mycophenolate mofetil [105], cyclosporine A [26,105], tacrolimus [28,105], prednisolone [105], sirolimus [105], nifedipine [105], fluconazole [105], voriconazole [29], itraconazole [32] and amphotericin B [30] does not significantly affect the plasma levels of micafungin [31].

Clinical efficacy
The efficacy of micafungin for the treatment of patients with esophageal candidiasis, invasive candidiasis and the prophylaxis of Candida spp. infections in patients undergoing HSCT was demonstrated in clinical Phase III trials.

- **Esophageal candidiasis**
The efficacy and safety of micafungin for the treatment of esophageal candidiasis has been evaluated in two double-blind studies. The first study compared the efficacy of micafungin (50, 100 and 150 mg/day) to fluconazole (200 mg/day) in patients with confirmed esophageal candidiasis (n = 245). It was demonstrated that micafungin at doses of 100 and 150 mg/day was more effective than at 50 mg/day. The efficacy of micafungin at dosages of 100 and 150 mg/day was comparable to that of fluconazole [33].

The noninferiority of micafungin 150 mg/day versus intravenous fluconazole 200 mg/day for the treatment of esophageal candidiasis was demonstrated in a large, randomized, double-blind trial with 518 patients. The overall therapeutic response rates were 87.3 and 87.2% for micafungin and fluconazole, respectively. No clinically meaningful differences in the incidence of possibly treatment-related adverse events between both treatment groups were observed. While patients in similar settings, treated with other echinocandins, such as caspofungin and anidulafungin, showed higher relapse rates than patients treated with fluconazole [34,35], no significant difference was observed between relapse rates of micafungin and fluconazole [36].

- **Prophylaxis of invasive fungal infections**
Another large, randomized, double-blind trial (n = 882) focused on the efficacy of micafungin preventing IFD in patients undergoing autologous (46%) or allogeneic (54%) HSCT. Patients either received micafungin 50 mg (1 mg/kg for patients weighing <50 kg) or fluconazole 400 mg (8 mg/kg for patients weighing <50 kg). The primary end point was treatment success, defined as the absence of proven, probable or suspected systemic fungal infection until the end of prophylaxis, as well as the absence of a proven or probable systemic fungal infection to the end of the 4 week post-treatment period. The overall success rate in preventing IFD was significantly higher in the micafungin arm compared with the fluconazole arm (80 vs 73.5%, respectively; p = 0.03). Patients in the micafungin arm needed significantly less empirical antifungal treatment compared with patients in the fluconazole arm (15.1 vs 21.4%; p = 0.02). There was a trend towards less breakthrough aspergillosis among patients treated with micafungin (one probable versus four proven and three probable cases for fluconazole; p = 0.07). However, since fluconazole is not the standard treatment for patients undergoing autologous HSCT, one should take note of the differences between the success rates with regard to the transplant type. While the treatment success rates for patients undergoing autologous HSCT were 89.2% for micafungin and 80.1% for fluconazole, the differences in the success rates for patients undergoing allogeneic HSCT were much smaller (71.4% for micafungin vs 68.4% for fluconazole) [37].

- **Candidemia & other invasive Candida infections**
A total of 148 (n = 126 per protocol) pediatric, neonatal and adult patients with newly diagnosed or refractory candidemia were enrolled in a non-comparative open-label study with micafungin alone and in combination with other antifungals. The daily doses of micafungin were 50 mg/day (1 mg/kg for patients <40 kg) for infections caused by C. albicans and 100 mg/day (2 mg/kg for patients <40 kg) for infections caused by other Candida species. Dose escalation was allowed. Success (complete or partial response) was observed in 83.3% of the patients per protocol population and serious adverse events related to micafungin were uncommon [7].
The efficacy of micafungin for the treatment of candidemia and other invasive Candida spp. infections has been studied in two randomized trials with either liposomal amphotericin B [38] or caspofungin [39] as the comparators.

Micafungin 100 mg was compared with liposomal amphotericin B (3 mg/kg) in a double-blind, randomized, multinational noninferiority study as the first-line treatment of candidemia and invasive candidiasis. While micafungin caused less adverse events than liposomal amphotericin B, the overall success rates were similar (74.1 and 69.6%, respectively). Hence, both compounds were equally effective for first-line treatment of candidemia and invasive candidiasis [38].

In a post-hoc analysis of the same study, the efficacy of micafungin versus liposomal amphotericin B was analyzed for intensive care unit (ICU) and non-ICU patients. In non-ICU patients, the treatment success rate was significantly higher among patients receiving micafungin than in those receiving liposomal amphotericin B (85 vs 72.1%, respectively; p = 0.0113). For ICU patients, the treatment success rates of micafungin and liposomal amphotericin B were similar (62.5 vs 66.4%, respectively), and lower than the corresponding treatment success rates of the non-ICU patients [40].

The efficacy of micafungin 100 and 150 mg for the treatment of candidemia and other forms of invasive candidiasis compared with caspofungin 50 mg was studied in another randomized, blinded trial with 595 patients. Of the 578 patients in the modified intent-to-treat population, 492 (85.1%) were diagnosed with candidemia, while the remainder had non-candidemia invasive candidiasis. At the end of the blinded therapy, the success rates of both echinocandins were equivalent (72.3, 76.4 and 71.4% for caspofungin 50 mg/day, micafungin 100 mg/day and micafungin 150 mg/day, respectively). No significant differences in mortality, relapse and emergent infections, or adverse events were observed between the study arms. Therefore, micafungin at both dosages (100 and 150 mg/day) was noninferior to a standard dosage of caspofungin [39].

■ Febrile neutropenia

Data on the efficacy and safety of micafungin in patients with hematological malignancies with fever resistant to broad-spectrum antibiotic therapy are limited, and are only based on noncomparative or retrospective studies. In a single-arm study with a small number of patients (32; of whom 23 fulfilled the protocol-defined criteria) the treatment success rate was 17 out of 23 (73.9%). None of the six patients who were considered treatment failures developed a documented fungal breakthrough infection, and discontinued the drug owing to lack of efficacy or died during the study period. One or more adverse events, of which none was above grade two toxicity, occurred in five (27.7%) patients [41]. The efficacy and safety of micafungin for the treatment of invasive fungal infections in patients with hematological malignancies (n = 277) was assessed in a noncomparative multicenter study with 197 evaluable patients, receiving 50–300 mg/day of micafungin. A total of 51 patients were diagnosed with FN (neutrophils below 500/µl) refractory to broad-spectrum antibacterial treatment (>48 h). A favorable response to micafungin was observed in 44 out of 51 (86.3%) of the patients diagnosed with FN. The response rates for patients diagnosed with probable, possible and suggested (fever refractory to antibacterial treatment) invasive fungal infections were 17 out of 38 (44.7%), 39 out of 63 (61.9%) and 71 out of 88 (80.7%), respectively [42].

A recently published sequential cohort analysis compared the efficacy of micafungin and caspofungin for the treatment of FN (n = 323). In this retrospective analysis, micafungin did not appear to differ significantly from caspofungin in terms of safety profile or efficacy [43].

■ Invasive aspergillosis

Data on the efficacy of micafungin for the treatment of aspergillosis only stem from single-armed studies.

The efficacy of micafungin, alone or in combination with other antifungals, as primary or salvage therapy for IA has been studied in a noncomparative open-label trial. However, the data of this trial are difficult to interpret since only few patients (n = 34), who fulfilled the diagnostic criteria for IA also received micafungin monotherapy. A favorable response to micafungin monotherapy was observed in six out of 12 (50%) and nine out of 22 (40.9%) patients in the primary therapy and the salvage therapy group, respectively. In combination with other antifungals, response rates were five out of 17 (29.4%) and 60 out of 174 (34.5%) for the primary and the salvage therapy groups, respectively [44].

In another noncomparative open-label trial, the efficacy and safety of micafungin for the treatment of deep-seated mycosis in Japanese patients was evaluated. Of 70 patients, 56 were evaluable
for efficacy, and received 12.5–150 mg/day of micafungin for up to 56 days. The overall clinical response rate in patients diagnosed with aspergillosis was 57% (24 out of 42 patients) [35], which roughly matches the rate of successful outcome (52.8%) observed in a double-blind study for voriconazole versus amphoterin B [46].

However, since comparative trials on micafungin for this indication have not been reported, micafungin has not been approved for the treatment of aspergillosis by either the FDA or the EMA [101,102].

A comparative Phase II trial on micafungin as salvage monotherapy for IA was recently stopped due to difficulties in recruitment and changes in the standard of care for IA [105]. At www.clinicaltrials.gov there is only one recruiting trial registered with micafungin for the treatment of aspergillosis, which has the objective to compare caspofungin with micafungin in adult Japanese patients with deep-seated Candida spp. or Aspergillus spp. infections [106].

Safety & tolerability
Micafungin, similar to other echinocandins, is a well-tolerated antifungal drug. The safety, tolerability and pharmacokinetic profile of micafungin was evaluated in a dose-escalation study in pediatric patients with FN (n = 77). The patients were stratified by age: 2–12 years (n = 57) and 13–17 years (n = 20). Therapy was initiated at 0.5 mg/kg/day and escalated to higher doses up to 4.0 mg/kg. The most common overall adverse events in the study population were diarrhea (19.5%), epistaxis (18.2%), abdominal pain (16.9%) and headache (16.9%). A moderate increase in liver-related laboratory parameters, possibly related to the study drug, was observed in two patients aged 13–17 years, who received micafungin 0.5 mg/kg/day. There was neither evidence of other toxicities, especially nephrotoxicity, nor any evidence of a dose-limiting toxicity [30].

The safety of micafungin was compared with that of fluconazole in patients with esophageal candidiasis and patients undergoing HSCT [33,36,37]. Neither of these studies revealed any clinical meaningful difference between micafungin and fluconazole in severe or serious adverse events. The most common treatment-related adverse events during the prophylaxis study for patients undergoing HSCT were gastrointestinal- (5.9% for micafungin vs 9.2% for fluconazole), hepatic- (5.2 vs 6.8%) and cardiovascular- (1.9 vs 3.1%) related adverse events. Fewer (p = 0.058) patients in the micafungin group (18; 4.2%) discontinued the study treatment owing to adverse events than in the fluconazole control group (33; 7.3%).

The safety of micafungin has also been evaluated in Phase III trials for the treatment of candidemia and other invasive Candida infections [38,39]. Compared with caspofungin, no significant difference of treatment-related adverse events was observed for micafungin at both dosages (100 and 150 mg/day) [39]. However, compared with liposomal amphoterin B, the safety profile of micafungin was better in terms of renal function, infusion-related events and electrolyte disturbances [38].

In a preclinical experiment, rats receiving micafungin for either 3 or 6 months at 32 mg/kg/day developed foci of altered hepatocytes and hepato-cellular tumors. Although the increase in carcinomas did not reach statistical significance, the persistence of altered hepatocellular foci subsequent to micafungin administration, and the presence of adenomas and carcinomas in the recovery periods suggest a causal relationship between micafungin sodium, altered hepatocellular foci and hepatic neoplasms [102]. Hence, the EMA, but not the FDA, included a warning in the label that micafungin should only be used if other antifungals are not appropriate. The decision to use micafungin should take into account the potential risk for the development of liver tumors [107].

Conclusion
Micafungin is a potent inhibitor of the 1,3-β-D-glucan synthase. Owing to its favorable profile for safety, tolerability and drug–drug interactions, micafungin has become an attractive option for the therapy of invasive candidiasis and azole-resistant esophageal candidiasis. Besides fluconazole, micafungin is the only drug that has been approved for Candida spp. prophylaxis in HSCT patients not undergoing high-dose immunosuppressive therapy for graft versus host disease. However, micafungin has not yet proven to be superior to current treatment options of choice, and since reliable clinical research on micafungin and its possible applications is coming along slowly, it has not yet been approved for the treatment of IA or fever of unknown origin.

Future perspective
Owing to its low interaction profile, micafungin is an interesting drug, especially for transplant patients in need of cyclosporine A, sirolimus or tacrolimus therapy. According to a recently published retrospective cohort study comparing caspofungin and micafungin in patients with
Micafungin in a nutshell: pharmacological & clinical aspects

Executive summary

Mechanism of action
- Micafungin inhibits fungal 1,3-β-D-glucan synthesis, causing severe damage to the fungal cell wall.
- Micafungin is fungicidal against almost all Candida spp. and fungistatic against many Aspergillus spp.

Pharmacokinetic properties
- Micafungin is only available as an intravenous solution owing to its poor bioavailability.
- Its long half-life allows once-daily administration.
- No dose adjustments are needed for intermediate hepatic or severe renal failure.
- No loading dose is required.
- Steady-state concentration is achieved after three doses.

Clinical efficacy
- Micafungin is noninferior for the treatment of esophageal candidiasis and invasive candidiasis.
- It has superior overall efficacy in preventing invasive fungal infections in hematopoietic stem cell transplantation patients.

Safety & tolerability
- No dose-limiting toxicity has yet been established.
- Few incidences of drug-induced toxicity.

Drug interaction
- Micafungin shows (only) marginal interactions with the cytochrome P450 (CYP3A4) system.
- Cyclosporine A clearance is slightly decreased by micafungin.
- Sirolimus and nifedipine area under the plasma concentration–time curve is slightly increased by micafungin.
- Micafungin does not interact with tacrolimus, rifampine and voriconazole.

Dosage & administration
- Available in 50 mg vials for preparation of intravenous solution.
- Dose: 50–150 mg administered once daily.

Bibliography

Papers of special note have been highlighted as:
- of interest

An interesting article on micafungin


**Websites**


102 Astellas Pharma US Inc. Mycamine® (label) [www.accessdata.fda.gov/drugsatfda_docs/label/2008/021506s008lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021506s008lbl.pdf)

103 Pfizer. Eraxis® (label) [www.accessdata.fda.gov/drugsatfda_docs/label/2006/021632s000,021948s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/021632s000,021948s000lbl.pdf)


105 Astellas Pharma OK, USA: Mycamine® product information [www.mycamine.com](http://www.mycamine.com)
