EUCAST technical note on anidulafungin

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Abstract

The European Committee on Antimicrobial Susceptibility Testing-Subcommittee on Antifungal Susceptibility Testing has determined breakpoints for anidulafungin for *Candida* spp. This Technical Note is based on the EUCAST anidulafungin rationale document (available at: http://www.eucast.org). Species-specific breakpoints for *C. albicans* are S ≤0.03 mg/L and R >0.03 mg/L and for *C. glabrata, C. tropicalis* and *C. krusei* S ≤0.06 mg/L and R >0.06 mg/L. *C. parapsilosis* was not regarded a good target for anidulafungin. There are insufficient data to set breakpoints for other species. The breakpoints are based upon pharmacokinetic data, epidemiological cut-off values and clinical experience. Breakpoints will be reviewed regularly.

Keywords: Anidulafungin, breakpoints, EUCAST Technical Note, susceptibility testing

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Anidulafungin is an echinocandin antifungal agent active against most *Candida* species. Anidulafungin is predominantly used for the treatment of disseminated candidiasis in non-neutropenic adult patients. Most data regarding anidulafungin *in vitro* susceptibility are derived from patients with candidaemia and a smaller number of patients with deep-seated organ infection.

The European Committee on Antimicrobial Susceptibility Testing-Subcommittee on Antifungal Susceptibility Testing (EUCAST-AFST) has determined breakpoints for anidulafungin for *Candida* spp. This Technical Note is based on the EUCAST anidulafungin rationale document (available on the EUCAST website: http://www.eucast.org). The rationale document includes more detail and published references related to the selection of EUCAST-AFST breakpoints (http://www.srga.org/eucastwt/MICTAB/EUCAST%20clinical%20MIC%20breakpoints%20-%20antimicrobials%20for%20Candida%20infections.htm).

The breakpoints are based on dosages of 200 mg/kg on day 1, then 100 mg/kg/day, and were established using MIC values from many sources. Wild-type isolates exhibit MICs of *C. albicans* ≤0.03 mg/L, *C. glabrata, C. krusei* and *C. tropicalis* ≤0.06 mg/L and *C. parapsilosis* ≤4 mg/L. Isolates with mutations in the hot spot regions of the target gene have been associated with clinical failures or breakthrough infections during echinocandin treatment [1–3]. The anidulafungin MICs of such mutant isolates are as follows: *C. albicans* >0.03 mg/L, *C. glabrata* >0.06 mg/L, *C. tropicalis* >0.06 mg/L and *C. krusei* >0.03 mg/L [4]. However, it should be noted that most of the data on breakthrough infections derive from studies with caspofungin as caspofungin has been in use the longest (approved in Europe in 2001, whereas anidulafungin was approved in 2007). The clinical data from three clinical trials were used [5–7]. These studies did not include MICs by the EUCAST method so a correlation of *in vitro* MICs with clinical outcome is not possible.

The EUCAST breakpoints (Table 1) are based on pharmacokinetic and microbiological data and clinical experience

TABLE 1. Species-specific anidulafungin EUCAST breakpoints

Species[a,b]	Species-related breakpoints[b,c] (mg/L)	
C. albicans	S ≤0.03	R >0.03
C. glabrata	S ≤0.06	R >0.06
C. tropicalis	S ≤0.06	R >0.06
C. krusei	S ≤0.06	R >0.06

[a]There is insufficient evidence to set non-species-related breakpoints.
[b]*C. parapsilosis* was considered a poor target for anidulafungin therapy and for that reason did not receive breakpoints. There is insufficient clinical evidence to set breakpoints for other species than those listed.
[c]MICs for *C. guilliermondii* are approximately 8 two-fold dilutions higher than those for *C. albicans*. There is insufficient evidence to indicate whether the wild-type population of this pathogen can be considered susceptible to anidulafungin. Hence, for *C. guilliermondii* there is insufficient evidence (IE) to set breakpoints.

[4–9]. Breakpoints for anidulafungin will be reviewed regularly. A number of *in vitro* studies on susceptibility of the fungus, of the target enzyme itself or in animal models have demonstrated cross-resistance between the three currently available echinocandins (anidulafungin, caspofungin and micafungin) for isolates with hot spot mutations in the target gene [3,10–15]. Hence, isolates categorized as anidulafungin susceptible can be regarded as susceptible to caspofungin and micafungin until drug-specific breakpoints are available for these two compounds.

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Transparency Declaration

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