# EUCAST technical note on posaconazole*

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## Abstract

The European Committee on Antimicrobial Susceptibility Testing-Subcommittee on Antifungal Susceptibility Testing (EUCAST-AFST) has determined breakpoints for posaconazole for *Candida* spp. This Technical Note is based on the EUCAST posaconazole rationale document (available on the EUCAST website: http://www.eucast.org). Species-specific breakpoints for *C. albicans, C. parapsilosis* and *C. tropicalis* are S: MIC ≤0.06 mg/L, R: MIC >0.06 mg/L. There are insufficient data to set breakpoints for *C. glabrata* and *C. krusei* as well as non-species-related breakpoints. The breakpoints are based upon pharmacokinetic data, epidemiological cut-off values and clinical experience. Breakpoints will be reviewed regularly.

**Keywords:** breakpoints, Candida, EUCAST Technical Note, Posaconazole, susceptibility testing

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## Introduction

Posaconazole is a triazole antifungal agent active *in vitro* against *Candida* spp. and *Cryptococcus* spp. as well as *Aspergillus* spp. and certain other moulds. The drug is approved for the following indications: (i) refractory invasive fungal diseases including aspergillosis, fusariosis, chromoblastomycosis, coccidioidomycosis and mycetoma, (ii) first-line therapy for the treatment of oropharyngeal candidiasis of patients who have severe disease or who are immunocompromized, for whom a response to topical therapy is expected to be poor and (iii) the prophylaxis of invasive fungal disease of patients receiving remission-induction chemotherapy for acute myelogenous leukaemia or myelodysplastic syndromes as well as for haematopoietic stem cell transplant recipients with graft vs. host disease.

The European Committee on Antimicrobial Susceptibility Testing-Subcommittee on Antifungal Susceptibility Testing (EUCAST-AFST) has determined breakpoints for posaconazole for *Candida* spp. This Technical Note is based on the EUCAST posaconazole 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 licensed dosing of 100 mg × 1, 200 mg × 3, 200 mg × 4 and 400 mg × 2 for mucosal infection and were established using MIC values from many sources. Wild-type isolates exhibits MICs of *C. albicans, C. parapsilosis* and *C. tropicalis* ≤0.064 mg/L, *C. glabrata* ≤1 mg/L, *C. krusei* ≤0.5 mg/L and *C. guilliermondii* ≤0.25 mg/L. The clinical data from four clinical trials on mucosal candidosis in HIV patients were used [1–3 and Data on File (Schering-Plough, Kenilworth, NJ, USA). The dataset included 488 *C. albicans*, 11 *C. glabrata*, 4 *C. krusei* and 3 *C. tropicalis*. MICs were determined by a reference laboratory. There were 448 (88.5%) successes and 58 (11.5%) failures. For *C. albicans* the rate of response was 89.3%. These studies did not include MICs by the EUCAST method so a

**TABLE 1. Species-specific Posaconazole EUCAST breakpoints**

| Species[a,b] | Species-related breakpoints[b] (mg/L) | |
|---|---|---|
| *C. albicans* | S ≤ 0.06 | R > 0.06 |
| *C. parapsilosis* | S ≤ 0.06 | R > 0.06 |
| *C. tropicalis* | S ≤ 0.06 | R > 0.06 |

[a]There is insufficient evidence to set non-species-related breakpoints.
[b]Epidemiological cut-off values for *C. glabrata, C. guilliermondii* and *C. krusei* are 1, 0.25 and 0. 5 mg/L, respectively, 2–4 two-fold dilutions higher than those for *C. albicans, C. parapsilosis* and *C. tropicalis.* In addition, the small number of cases in the clinical trials means that there is insufficient evidence to indicate whether the wild-type populations of these pathogens can be considered as susceptible to posaconazole. Hence, for *C. glabrata, C. guilliermondii* and *C. krusei* there is insufficient evidence to set breakpoints.

correlation of *in vitro* MICs with clinical outcome is not possible. Furthermore, there is no clinical evidence that cases involving isolates with acquired resistance mechanisms respond to treatment, hence the EUCAST breakpoints, which are summarized in Table 1, are based upon pharmacokinetic data, epidemiological cut-off values and clinical experience [1–6]. Breakpoints will be reviewed regularly.

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## Transparency Declaration

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