# European Committee on Antimicrobial Susceptibility Testing

## Antifungal Agents

## Breakpoint tables for interpretation of MICs

Version 5.0, valid from 2013-01-09


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Version 5.0, valid from 2013-01-09

**Notes**

1. The EUCAST tables of clinical breakpoints for antifungal agents contain clinical MIC breakpoints determined over the period 2007-2012.

2. Numbered footnotes relating to MIC breakpoints are listed in a column on the right of the spreadsheet rather than below the table.

3. Highlighted names of antifungal agents link to EUCAST rationale documents. Highlighted MIC breakpoints link to EUCAST MIC distributions.

4. One version of the document is released as an unprotected Excel file to enable users to alter the list of agents to suit the range of agents tested locally and to present breakpoints in the format used locally. The content of single cells cannot be changed.
Hide lines by right-clicking on the line number and choosing "hide".
Hide columns by right-clicking on the column letter and choosing "hide".
If you wish to add the intermediate columns for MICs and/or zone diameters right-click on the column letter and choose "insert". The intermediate values are inferred from the "S" and "R" breakpoints.

5. In order to simplify the EUCAST tables, the intermediate category is not listed. It is readily interpreted as the values between the S and the R breakpoint. For example, for MIC breakpoints listed as S ≤ 1 mg/L and R > 8 mg/L, the intermediate category is 2-8 (technically >1-8) mg/L.

"-" indicates that susceptibility testing is not recommended as the species is a poor target for therapy with the drug. Isolates may be reported as R without prior testing.

"IE" indicates that there is insufficient evidence that the species in question is a good target for therapy with the drug. An MIC with a comment but without an accompanying S, I or R categorisation may be reported.

NA = Not Applicable

IP = In Preparation

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## Antifungal Agents

## Breakpoint tables for interpretation of MICs

Version 5.0, valid from 2013-01-09

| Table | Changes from version 4.1 (Changes are marked with yellow highlights) |
|---|---|
| **Notes** | Typo corrected in Note 1 (2002 changed to 2007). |
| **General** | Links added to rationale documents and MIC distributions (not shown as yellow highlights). |
| ***Aspergillus* spp.** | Voriconazole breakpoints added.<br>Comment 4 revised (itraconazole changed to azole). |

## *Candida* spp.

## EUCAST Antifungal Clinical Breakpoint Table v. 5.0, valid from 2013-01-09

**MIC method (EUCAST standardised broth microdilution method)**
**Medium:** RPMI1640-2% glucose, MOPS buffer
**Inoculum:** Final $0.5x10^5$ – $2.5x10^5$ cfu/mL
**Incubation:** 18-24h
**Reading:** Spectrophotometric, full inhibition for amphotericin B but 50% growth inhibition for other compounds
**Quality control:** *C. parapsilosis* ATCC 22019 or *C. krusei* ATCC 6258

| Antifungal agent | MIC breakpoint (mg/L) | | | | | | | | | | | | | | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *C. albicans* | | *C. glabrata* | | *C. krusei* | | *C. parapsilosis* | | *C. tropicalis* | | *C. guilliermondii* | | Non-species related breakpoints[1] | | |
| | S ≤ | R > | S ≤ | R > | S ≤ | R > | S ≤ | R > | S ≤ | R > | S ≤ | R > | S ≤ | R > | |
| | | | | | | | | | | | | | | | **1.** Non-species related breakpoints have been determined mainly on the basis of PK/PD data and are independent of MIC distributions of specific species. They are for use only for organisms that do not have specific breakpoints. |
| **Amphotericin B** | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | IE | IE | IE | IE | |
| **Anidulafungin** | 0.03 | 0.03 | 0.06 | 0.06 | 0.06 | 0.06 | - | - | 0.06 | 0.06 | IE[2] | IE[2] | IE | IE | **2.** The ECOFFs for these species are in general higher than for *C. albicans*. |
| **Caspofungin** | Note[3] | Note[3] | Note[3] | Note[3] | Note[3] | Note[3] | - | - | Note[3] | Note[3] | IE[2] | IE[2] | IE | IE | **3.** Due to significant inter-laboratory variation in MIC ranges for caspofungin, EUCAST breakpoints have not yet been established. |
| **Fluconazole** | 2 | 4 | IE[2] | IE[2] | - | - | 2 | 4 | 2 | 4 | IE[2] | IE[2] | 2 | 4 | |
| **Itraconazole** | IP | IP | IP | IP | IP | IP | IP | IP | IP | IP | IP | IP | IP | IP | |
| **Micafungin** | IP | IP | IP | IP | IP | IP | - | - | IP | IP | IE[2] | IE[2] | IP | IP | |
| **Posaconazole** | 0.06 | 0.06 | IE[2] | IE[2] | IE[2] | IE[2] | 0.06 | 0.06 | 0.06 | 0.06 | IE[2] | IE[2] | IE | IE | |
| **Voriconazole** | 0.12[4] | 0.12[4] | IE | IE | IE | IE | 0.12[4] | 0.12[4] | 0.12[4] | 0.12[4] | IE[2] | IE[2] | IE | IE | **4.** Strains with MIC values above the S/I breakpoint are rare or not yet reported. The identification and antimicrobial susceptibility tests on any such isolate must be repeated and if the result is confirmed the isolate sent to a reference laboratory. Until there is evidence regarding clinical response for confirmed isolates with MIC above the current resistant breakpoint (in italics) they should be reported resistant. |

## *Aspergillus* spp.

## EUCAST Antifungal Clinical Breakpoint Table v. 5.0, valid from 2013-01-09

**MIC method (EUCAST standardised broth microdilution method)**
**Medium:** RPMI1640-2% glucose, MOPS as buffer
**Inoculum:** Final 1x10(5) – 2.5x10(5) cfu/mL
**Incubation:** 48h
**Reading:** Visual
**Quality control:** *A. fumigatus* ATCC 204305, *A. flavus* ATCC 204304, *A. fumigatus* F 6919, *A. flavus* CM 1813, *C. parapsilosis* ATCC 22019 (read after 18-24 h) or *C. krusei* ATCC 6258 (read after 18-24 h)

| Antifungal agent | MIC breakpoint (mg/L) | | | | | | | | | | | | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *A. flavus* | | *A. fumigatus* | | *A. nidulans* | | *A. niger* | | *A. terreus* | | Non-species related breakpoints[1] | | |
| | S ≤ | R > | S ≤ | R > | S ≤ | R > | S ≤ | R > | S ≤ | R > | S ≤ | R > | |
| | | | | | | | | | | | | | **1.** Non-species related breakpoints have been determined mainly on the basis of PK/PD data and are independent of MIC distributions of specific species. They are for use only for organisms that do not have specific breakpoints. |
| **Amphotericin B** | IE[2] | IE[2] | 1 | 2 | Note[3] | Note[3] | 1 | 2 | - | - | IE | IE | **2.** The ECOFFs for these species are in general one step higher than for *A. fumigatus.* **3.** There are too few MIC data to establish ECOFFs and hence to suggest any breakpoints. |
| **Anidulafungin** | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | |
| **Caspofungin** | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | |
| **Fluconazole** | - | - | - | - | - | - | - | - | - | - | - | - | |
| **Itraconazole[4]** | 1 | 2 | 1 | 2 | 1 | 2 | IE[2,5] | IE[2,5] | 1 | 2 | IE[5] | IE[5] | **4.** Monitoring of azole trough concentrations in patients treated for fungal infection is recommended. **5.** The MIC values for isolates of *A. niger* and *A. versicolor* are in general higher than those for *A. fumigatus* . Whether this translates into a poorer clinical response is unknown. |
| **Micafungin** | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | |
| **Posaconazole[4]** | IE[2] | IE[2] | 0.12[6] | 0.25[6] | IE[2] | IE[2] | IE[2] | IE[2] | 0.12[6] | 0.25[6] | IE | IE | **6.** Provided adequate drug exposure has been confirmed using therapeutic drug monitoring (TDM). There remains some uncertainty regarding cut-off values for posaconazole concentrations that separate patients with a high probability of clinical success from those with a low probability of clinical success. In some circumstances (e.g. patients with persistent and profound neutropenia, large lesions, or those with other features associated with a poor clinical outcome) a relatively high trough concentration should be sought. Preclinical and clinical data suggest this value should be >1 mg/L at steady state. For other patient groups a lower trough concentration may be acceptable. For prophylaxis a target concentration of >0.7 mg/L has been suggested. |
| **Voriconazole[4]** | IE[2] | IE[2] | 1 | 2 | IE | IE | IE[2] | IE[2] | IE[2] | IE[2] | IE | IE | |