EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

European Committee on Antimicrobial Susceptibility Testing

Breakpoint tables for interpretation of MICs for antifungal agents

Version 11.0, valid from 2024-12-02

Content	Page	
Notes	1	
Guidance on reading EUCAST antifungal breakpoint tables	3	
Information on technical uncertainty	4	
Changes	5	
Candida and *Cryptococcus* spp.	6	
Aspergillus spp.	8	
Dosages	9	
Antimicrobial susceptibility tests on groups of organisms or agents for which there are no EUCAST breakpoints		Link to Guidance document for interpretation of MICs for yeasts when there are no breakpoints

This document should be cited as: “The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs for antifungal agents, version 11.0, 2024. http://www.eucast.org/astoffungi/clinicalbreakpointsforantifungals/.

European Committee on Antimicrobial Susceptibility Testing

Breakpoint tables for interpretation of MICs for antifungal agents

Version 11.0, valid from 2024-12-02

Notes

1. The EUCAST tables of clinical breakpoints for antifungal agents contain clinical MIC breakpoints determined over the period **2007-2024**. The EUCAST breakpoint table version **11.0** includes corrected typographical errors, clarifications, breakpoints for new agents and/or organisms, and revised MIC breakpoints. Changes are best seen on screen or on a colour printout since cells containing a change are yellow.

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

3. Antifungal agents names in blue link to EUCAST rationale documents. MIC breakpoints in blue link to EUCAST MIC distributions.

4. The document is released as a protected Excel® file suitable for viewing on screen and as an Acrobat® pdf file for printing. To utilise all functions in the Excel® file, use Microsoft™ original programs only. The Excel® file enables users to alter the list of agents to suit the local range of agents tested 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 right-click on the column letter and choose "insert". The intermediate values are inferred from the "S" and "R" breakpoints when not specified in the table.

5. EUCAST breakpoints are used to categorise results into three susceptibility categories:
S - Susceptible, standard dosing regimen: A microorganism is categorised as *Susceptible, standard dosing regimen,* when there is a high likelihood of therapeutic success using a standard dosing regimen of the agent.
I - Susceptible, increased exposure: A microorganism is categorised as *Susceptible, increased exposure** when there is a high likelihood of therapeutic success because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection.
R - Resistant: A microorganism is categorised as *Resistant* when there is a high likelihood of therapeutic failure even when there is increased exposure.
*Exposure is a function of how the mode of administration, dose, dosing interval, infusion time, as well as distribution and excretion of the antimicrobial agent will influence the infecting organism at the site of infection.

6. For some organism-agent combinations, results may be in an area where the interpretation is uncertain. EUCAST has designated this an Area of Technical Uncertainty (ATU). It corresponds to an MIC value where the categorisation is doubtful. See separate page (Technical uncertainty) for more information on ATU and how to deal with results in the ATU.

7. In order to simplify the EUCAST tables, the I 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 I category is 2-8 (technically >1-8) mg/L.

Notes

8. By international convention MIC dilution series are based on twofold dilutions up and down from 1 mg/L. At dilutions below 0.25 mg/L, this leads to concentrations with multiple decimal places. To avoid having to use these in tables and documents, EUCAST has decided to use the following format (in bold): 0.125→**0.125**, 0.0625→**0.06**, 0.03125→**0.03**, 0.015625→**0.016**, 0.0078125→**0.008**, 0.00390625→**0.004** and 0.001953125→**0.002** 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

EUCAST Antifungal Clinical Breakpoint Table v. 11.0, valid from 2024-12-02

The I category is not listed but is interpreted as the values between the S and the R breakpoints. If the S and R breakpoints are the same value there is no I category.

Agent A: No I category
Agent B: I category: 4 mg/L
Agent G: I category: 1-2 mg/L

Area of Technical Uncertainty
See specific information on how to handle technical uncertainty in antimicrobial susceptibility testing.

Insufficient evidence that the organism or group is a good target for therapy with the agent

No breakpoints. Susceptibility testing is not recommended

Changes from previous version highlighted in yellow

Antifungal agent	MIC breakpoint (mg/L)		
	MIC breakpoint (mg/L)		
	S ≤	R >	ATU
Antimicrobial agent A	1[1]	1[1]	
Antimicrobial agent B	2[2]	4	
Antimicrobial agent C	IE	IE	
Antimicrobial agent D	-	-	
Antimicrobial agent E	IP	IP	
Antimicrobial agent F	NA	NA	
Antimicrobial agent G	0.5	2	
Antimicrobial agent H	0.001	1	

In Preparation

Notes. Numbered notes relate to general comments and/or MIC breakpoints.
1. Notes that are general comments and/or relating to MIC breakpoints.
2. New comment
~~Removed comment~~

MIC breakpoints in blue are linked to MIC distributions

Not Applicable

Antifungal agents in blue are linked to EUCAST rationale documents

An arbitrary "off scale" breakpoint which categorises wild-type organisms as "Susceptible - increased exposure"

European Committee on Antimicrobial Susceptibility Testing

Breakpoint tables for interpretation of MICs for antifungal agents

Version 11.0, valid from 2024-12-02

How to handle technical uncertainty in antimicrobial susceptibility testing

All measurements are affected by random variation and some by systematic variation. Systematic variation should be avoided and random variation reduced as much as possible. Antimicrobial susceptibility testing (AST), irrespective of method, is no exception.

EUCAST strives to minimise variation by providing standardised methods for MIC determination and disk diffusion and by avoiding setting breakpoints which seriously affect the reproducibility of the test. Variation in AST can be further reduced by setting more stringent standards for manufacturers of AST material (growth medium and antifungals) and criteria for quality control of manufacturing processes and laboratory practices.

It is tempting to think that generating an MIC value will solve all problems. However, MIC measurements also have variation and a single value is not automatically correct. Even when using the reference method, MICs vary between days and technicians. Under the best of circumstances, an MIC of 1.0 should be considered as a value between 0.5 and 2.0 mg/L. Not infrequently, there are problems with commercial testing systems including broth microdilution tests, gradient tests and semi-automated AST devices.

Although AST in principle is straightforward for most agents and species, there are problematic areas. It is important to warn laboratories about these and the uncertainty of susceptibility categorisation. Analysis of EUCAST data that have been generated over the years has identified such situations, called **Areas of Technical Uncertainty (ATU)**. The ATUs are **warnings to laboratory staff** that there is an uncertainty that needs to be addressed before reporting AST results to clinical colleagues. The ATU is not to be conveyed to clinical colleagues except under special circumstances and only as part of a discussion about therapeutic alternatives in difficult cases.

Below are alternatives for how the ATUs can be dealt with by the laboratory. Which of these actions are chosen will depend on the situation. The type of sample (f.x. blood culture vs. mucosal culture), the number of alternative agents available, the severity of the disease, whether or not a consultation with clinical colleagues is feasible, will influence the action taken.

- **Repeat the test**

  This is only relevant if there is reason to suspect a technical error in the primary AST.

- **Use an alternative test (perform a genotypic test)**

  This may be relevant if the susceptibility report leaves only few therapeutic alternatives or if the result is deemed of importance. If the organism is multi-resistant, it is advisable to perform a genotypic characterization of the resistance mechanism to obtain more information (examples: *FKS* gene sequencing in *Candida* and *CYP51A* gene sequencing in *A. fumigatus*).

- **Downgrade the susceptibility category**

  If there are other therapeutic alternatives in the AST report, it is permissible to downgrade the result (from S to I, or from I to R or from S to R). However, a comment should be included and the isolate saved for further testing.

- **Upgrade the susceptibility category**

  If there are substantial evidence that the isolate will be clinically susceptible (for example in isolates with a one-step MIC elevation above the susceptibility breakpoint AND absence of FKS mutations in a *Candida* isolate with susceptible phenotype to alternative candins, or an *A. fumigatus* isolate with an MIC of 0.25 mg/L for posaconazole but susceptible to itraconazole) it is permissible to upgrade the result (from R to S, or from I to S). However, a comment should be included and the isolate saved for further testing. Such a comment could be: "based upon clinical experience the isolate will be clinically susceptible to drug x despite the one-step elevated MIC".

- **Include the uncertainty as part of the report**

  It is common practice in many other laboratory settings to include information on the uncertainty of the reported result. This can be dealt with in several alternative ways:

  * For serious situations, take the opportunity to contact the clinical colleagues to explain and discuss the results.

* Categorise the result according to the breakpoints but include information about the technical difficulties and/or the uncertainty of the interpretation. In many instances, a straight “R” is less ambiguous than other alternatives, especially when there are alternative agents.

The Area of Technical Uncertainty will typically be listed as a defined MIC value. ATUs will only be listed when obviously needed. The absence of an ATU (MIC) means that there is no immediate need for a warning. The ATUs introduced in 2019 (v. 10.0) will be evaluated and ATUs may be added as more information develops.

Link to the guidance material available on the EUCAST website.

European Committee on Antimicrobial Susceptibility Testing

Breakpoint tables for interpretation of MICs for antifungal agents

Version 11.0, valid from 2024-12-02

Version 11.0, 2024-12-02	**Changes (cells containing a change, a deletion or an addition) from v. 10.0 are marked yellow.** **New or changed comments are underlined. Removed comments are shown in strikethrough font style.**
General	The column title "Comments on the ATU" has been revised on both the candida and aspergillus sheets and now simply read "Comments"
***Candida* and *Cryptococcus* spp.**	The anidulafungin breakpoint has been lowered one dilution for *Candida albicans* and established for *C. dubliniensis*. The micafungin breakpoint for *C. albicans* has been increased one dilution and the ATU removed. Additionally breakpoints have been established for *C. dubliniensis* and *C. tropicalis.* Breakpoints for rezafungin and *C. albicans, C. dubliniensis, C. glabrata, C. krusei, C. parapsilosis* and *C. tropicalis* have established and included. It is important to note, that the rezafungin breakpoints apply for MICs determined with the modified EUCAST methodology using Tween 20 supplemented growth medium (final concentration 0.002%) as described specifically for rezafungin in the E.Def 7.4 method document. Included reference to the "What to do when there are no breakpoints, rare yeast" document for the species where pragmatic recommendations are available (*C. guilliermondii, C. lusitaniae, S. cerevisiae; C. kefyr*).
***Aspergillus* spp.**	The former ATUs for itraconazole and voriconazole of 2 mg/L have been omitted, as they did not represent classification uncertainty dependent on technical issues. However, the agents may be used in some special situations where no other alternatives are available for treating chronic pulmonary aspergillosis, provided high exposure is obtained and ensured via therapeutic drug monitoring is acknowledged and advice included regarding reporting of isolates with MIC 2 mg/L.
Dosages	Dosage recommendation has been provided for rezafungin

Candida and *Cryptococcus* spp.

EUCAST Antifungal Clinical Breakpoint Table v. 11.0, valid from 2024-12-02

For species not in the table, please consult: **Guidance for interpretation of MICs for yeasts when there are no breakpoints**

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, complete (>90%) 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)																			Comments on the I category	Comments
	Candida albicans			*Candida dubliniensis*		*Candida glabrata*		*Candida krusei*		*Candida parapsilosis*		*Candida tropicalis*		*Candida guilliermondii*		*Cryptococcus neoformans*		Non-species related breakpoints for *Candida*[1]			
	S ≤	R >	ATU	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >		
Amphotericin B	1	1		1	1	1	1	1	1	1	1	1	1	IE	IE	1	1	IE	IE	No data to support an I category according to the new definitions	
Anidulafungin	0.016	0.016		0.03	0.03	0.06	0.06	0.06	0.06	4	4	0.06	0.06	IE	IE	-	-	IE	IE		
Caspofungin	Note[3]	Note[3]		IE	IE	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	IE	IE	-	-	IE	IE		
Fluconazole	2	4		2	4	0.001[4]	16	-	-	2	4	2	4	IE[2]	IE[2]	IE	IE	2	4	See dosages table for appropriate dose	
Isavuconazole	IE	IE		IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE		
Itraconazole	0.06	0.06		0.06	0.06	IE[2]	IE[2]	IE[2]	IE[2]	0.125	0.125	0.125	0.125	IE[2]	IE[2]	IE	IE	IE	IE		
Micafungin	0.03	0.03		0.06	0.06	0.03	0.03	IE[5]	IE[5]	4	4	0.06	0.06	IE[5]	IE[5]	-	-	IE	IE		
Posaconazole	0.06	0.06		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	IE	IE		
Rezafungin	0.008	0.008		0.016	0.016	0.016	0.016	0.03	0.03	4	4	0.03	0.03	IE	IE	-	-	IE	IE		Breakpoints apply for MICs determined with Tween 20 supplemented medium according to the EUCAST E.Def 7.4 method.
Voriconazole[6]	0.06	0.25[7]		0.06[7]	0.25[7]	IE[2]	IE[2]	IE[2]	IE[2]	0.125[7]	0.25[7]	0.125[7]	0.25[7]	IE	IE	IE	IE	IE	IE	4 mg/kg iv twice daily	

Notes

Candida and *Cryptococcus* spp.

EUCAST Antifungal Clinical Breakpoint Table v. 11.0, valid from 2024-12-02

For species not in the table, please consult: **Guidance for interpretation of MICs for yeasts when there are no breakpoints**

1. Non-species related breakpoints have been determined mainly on the basis of PK/PD data and are independent of MIC distributions of specific *Candida* species. They are for use only for organisms that do not have specific breakpoints.

2. The ECOFFs for these species are in general higher than for *C. albicans.*

3. Isolates that are susceptible to anidulafungin as well as micafungin should be considered susceptible to caspofungin, until caspofungin breakpoints have been established. EUCAST breakpoints have not yet been established for caspofungin, due to significant inter-laboratory variation in MIC ranges for caspofungin.

4. The entire *C. glabrata* is in the I category. MICs against *C. glabrata* should be interpreted as resistant when above 16 mg/L. Susceptible category (≤0.001 mg/L) is simply to avoid missclassification of "I" strains as "S" strains.

5. MICs for *C. tropicalis* are 1-2 two-fold dilution steps higher than for *C. albicans* and *C. glabrata*. In the clinical study successful outcome was numerically slightly lower for *C. tropicalis* than for *C. albicans* at both dosages (100 and 150 mg daily). However, the difference was not significant and whether it translates into a relevant clinical difference is unknown. MICs for *C. krusei* are approximately three two-fold dilution steps higher than those for *C. albicans* and, similarly, those for *C. guilliermondii* are approximately eight two-fold dilutions higher. In addition, there were only a small number of cases involved these species in the clinical trials. This means there is insufficient evidence (IE) to indicate whether the wild-type population of these pathogens can be considered susceptible to micafungin.

6. For *Candida* the I category is introduced to acknowledge that the increased exposure obtained by iv dosing is sufficient (potentially confirmed by TDM). There is not enough information available for the response to voriconazole of infections caused by *Candida* isolates with higher MICs.

7. Strains with MIC values above the S/I breakpoint are rare or not yet reported. The identification and antifungal 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 they should be reported resistant. A clinical response of 76% was achieved in infections caused by the species listed below when MICs were lower than or equal to the epidemiological cut-offs. Therefore, wild type populations of *C. albicans, C. dubliniensis, C. parapsilosis* and *C. tropicalis* are considered susceptible.

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, complete inhibition for amphotericin B and azoles (MIC), aberrant growth endpoint for echinocandins (MEC).
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)																Comments on the I category	Comments
	A. flavus			*A. fumigatus*			*A. nidulans*			*A. niger*		*A. terreus*			Non-species related breakpoints[1]			
	S ≤	R >	ATU	S ≤	R >	ATU	S ≤	R >	ATU	S ≤	R >	S ≤	R >	ATU	S ≤	R >		
Amphotericin B	-	-		1	1		-	-		1	1	-	-		IE	IE	No data to support an "I" category according to the new definition of "I"	
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	-	-		-	-		-	-		-	-	-	-		-	-		
Isavuconazole	1	2	2	1	2	2	0.25	0.25		IE[2]	IE[2]	1	1		IE	IE	Isavuconazole MIC = 2 mg/L should not be interpreted as I but only followed up as an ATU	If voriconazole wild-type (*A. flavus*: voriconazole MIC ≤2 mg/L; *A. fumigatus*: voriconazole MIC ≤1 mg/L) report as isavuconazole S and add the following comment: The MIC of 2 mg/L is one dilution above the S breakpoint but within the wild-type isavuconazole MIC range due to a stringent breakpoint susceptibility breakpoint. See rationale documents for more information. If voriconazole non wild-type report as isavuconazole R and refer to reference laboratory for *CYP51A* sequencing and confirmation of MICs[3]."
Itraconazole[4]	1	1		1	1		1	1		IE[2,5]	IE[2,5]	1	1		IE[5]	IE[5]		For isolates with confirmed MIC 2 mg/L (one dilution above the breakpoint), itraconazole may be considered for treatment of chronic pulmonary aspergillosis when no alternative is available and when sufficient exposure (>2 mg/L) is ensured via TDM.
Micafungin	IE	IE		IE	IE		IE	IE		IE	IE	IE	IE		IE	IE		
Posaconazole[4]	IE[2]	IE[2]		0.125	0.25	0.25	IE[2]	IE[2]		IE[2]	IE[2]	0.125	0.25	0.25	IE	IE	Posaconazole MIC = 0.25 mg/L should not be interpreted as I but only as ATU	If S to itraconazole report as S and add the following comment: "The MIC is 0.25 mg/L and thus one dilution above the S breakpoint due to overlapping wt and non-wt populations". If not S to itraconazole report as R and refer to reference laboratory for *CYP51A* sequencing and confirmation of MICs.
Voriconazole[4]	IE[2]	IE[2]		1	1		1	1		IE[2]	IE[2]	IE[2]	IE[2]		IE	IE		For isolates with confirmed MIC 2 mg/L (one dilution above the breakpoint), voriconazole may be considered for treatment of chronic pulmonary aspergillosis when no alternative is available and when sufficient exposure (>2-3 mg/L) is ensured via TDM.

Notes

1. Non-species related breakpoints have not been determined.

2. The ECOFFs for these species are in general one two-fold dilution higher than for *A. fumigatus*.

3. Itraconazole and posaconazole R isolates but S to voriconazole and isavuconazole are not uncommon in azole-treated patients. Refer the isolate to a reference laboratory for *CYP51A* sequencing and confirmation of MICs.

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.

Dosages

EUCAST breakpoints are based on the following adult dosages (see section 8 in Rationale Documents). Alternative dosing regimens which result in equivalent exposure are acceptable. The table should not be considered an exhaustive guidance for dosing in clinical practice, and does not replace specific local, national, or regional dosing guidelines.

Note: duration of treatment only indicated for loading doses, because the total duration of therapy is not only dependent on the type and site of infection but also on the underlying disease of the patient. Please consult clinical management guidelines for recommendations on total duration.

Azoles	Standard dose	Increased Exposure Dose	Special situations
Fluconazole	800 mg x 1 for first day followed by 400 mg x 1 iv/oral (or 6 mg/kg)	800 mg x 1 iv/oral (or 12 mg/kg)	Indicated doses are those appropriate for invasive candidiasis Mucosal infections (Mendling et al; Mycoses. 2012;55 Suppl 3:1-13): Standard doses is 100-200 mg x 1 and increased dose 800 mg x 1 (for *C. glabrata*)
Itraconazole	200 mg x 2 for first day followed by 100*-400** mg iv/po Target trough level***: >0.5 mg/L for prophylaxis, >1 mg/L for therapy		*Superficial infections only **Daily doses up to 200 mg x 2 may be given depending on the infection. Capsules have 30% lower bioavailability than the oral solution ***HPLC assay method and Parent compound only.
Isavuconazole	200 mg x 3 for first 2 days followed by 200 mg x 1 iv/oral		
Posaconazole	Tablets/iv: 300 mg x 2 for first day followed by 300 mg x 1 Oral suspension: 200 mg x 4 for first day or 400 mg x 2 Target trough level: >0.7 mg/L for prophylaxis and >1.25 mg/L for therapy		
Voriconazole	6 mg/kg x 2 for first day followed by 4 mg/kg x 2 iv 400 mg x 2 for first day followed by 200 mg x 2 po Target trough level: >0.5 mg/L for prophylaxis, 2-5.5 mg/L for therapy	*Candida* : The I-category only applies for the iv dosage (not the standard oral dose)	Increased exposure can be achieved by elevated dosage (note non-linear kinetics in adults) or with a proton pump inhibitor, in patients with low blood levels.

Amphotericin B formulations	Standard dose	Increased Exposure Dose	Special situations
Liposomal amphotericin B	3 mg/kg x 1		Increased doses up to 7 mg/kg (or even 10 mg/kg e.g. *Mucorales* CNS infections) can be used in specific situations.
Amphotericin B deoxycholate	1 mg/kg x 1		
ABLC	5 mg/kg x1		

Echinocandins	Standard dose	Increased Exposure Dose	Special situations
Anidulafungin	200 mg x 1 for first day followed by 100 mg x 1		
Caspofungin	70 mg x 1 for first day followed by 50* mg x 1 (weight ≤ 80 kg) 70 mg x 1 (weight > 80 kg)		
Micafungin	100 mg x 1 (weight >40 kg) 2 mg/kg x 1 in patients weighing <40 kg		Increased dose indicated in patients not responding to standard dose: 200 mg x 1 (weight >40 kg), or 4 mg/kg x 1 in patients weighing <40 kg. Standard dose for chronic aspergillosis is Micafungin 150 mg x 1 (Chronic pulmonary aspergillosis: rationale and clinical guidelines for diagnosis and management. Eur Resp J 2016).
Rezafungin	400 mg x 1 for first day followed by 200 mg x 1 weekly		