

## European Committee on Antimicrobial Susceptibility Testing

### Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.3 and E.Def 11.0 procedures

Version 2.0, valid from 2020-09-24

**This document should be cited as**

"The European Committee on Antimicrobial Susceptibility Testing. Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.3 and E.Def 11.0 procedures. Version 2, 2020. <http://www.eucast.org>."

<b>General</b>	<b>Page</b>
Changes	1
Clinical breakpoints and ECOFFs for yeasts	2
Clinical breakpoints and ECOFFs for moulds	5
Clinical breakpoints and ECOFFs for dermatophytes	9

# European Committee on Antimicrobial Susceptibility Testing

Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.3 and E.Def 11.0 procedures

Version 2.0, valid from 2020-09-24

<b>Version 2.0, valid from 2020-09-24</b>	<b>Changes</b> Cells containing a change or an addition from the "Overview of antifungal..." document v. 1.0 are marked yellow (Format changes are not marked yellow)
Content	Title revised in order to include dermatophytes
4. Dermatophytes	This new sheet has been added summarising tentative ECOFFs for <i>T. interdigitale</i> and <i>T. rubrum</i> .

Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.3 and E.Def 11.0 procedures

Version 2.0, valid from 2020-09-24

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
<i>C. albicans</i>	Amphotericin B	1	1			1	
	Anidulafungin	0.03	0.03			0.03	
	Micafungin	0.016	0.016			0.016	0.03
	Fluconazole	0.5	2	4		4	
	Itraconazole	0.06	0.06			0.06	
	Posaconazole	0.06	0.06			0.06	
	Voriconazole	0.03	0.06	0.125-0.25		0.25	
	Isavuconazole	ND	ND			ND	
<i>C. dubliniensis</i>	Amphotericin B	0.25	1			1	
	Anidulafungin	ND					
	Micafungin	ND					
	Fluconazole	[0.5]*	2	4		4	
	Itraconazole	0.06	0.06			0.06	
	Posaconazole	0.06	0.06			0.06	
	Voriconazole	0.03	0.06	0.125-0.25		0.25	
	Isavuconazole	ND	ND			ND	
<i>C. glabrata</i>	Amphotericin B	1	1			1	
	Anidulafungin	0.06	0.06			0.06	
	Micafungin	0.03	0.03			0.03	
	Fluconazole	16	0.001	≤16		16	
	Itraconazole	2	ND			ND	
	Posaconazole	1	ND			ND	
	Voriconazole	1	ND			ND	
	Isavuconazole	ND	ND			ND	
<i>C. krusei</i>	Amphotericin B	1	1			1	
	Anidulafungin	0.06	0.06			0.06	
	Micafungin	0.25	ND			ND	
	Fluconazole	128	ND			ND	
	Itraconazole	1	ND			ND	
	Posaconazole	0.5	ND			ND	
	Voriconazole	1	ND			ND	
	Isavuconazole	ND	ND			ND	

Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.3 and E.Def 11.0 procedures

Version 2.0, valid from 2020-09-24

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
<i>C. parapsilosis</i>	Amphotericin B	1	1		1		
	Anidulafungin	4	4		4		
	Micafungin	2	2		2		
	Fluconazole	2	2	4	4		
	Itraconazole	0.125	0.125		0.125		
	Posaconazole	0.06	0.06		0.06		
	Voriconazole	0.06	0.125	0.25	0.25		
	Isavuconazole	ND	ND		ND		
<i>C. tropicalis</i>	Amphotericin B	1	1		1		
	Anidulafungin	0.06	0.06		0.06		
	Micafungin	0.06	ND		ND		
	Fluconazole	1	2	4	4		
	Itraconazole	0.125	0.125		0.125		
	Posaconazole	0.06	0.06		0.06		
	Voriconazole	0.125	0.125	0.25	0.25		
	Isavuconazole	ND	ND		ND		
<i>C. guilliermondii</i>	Amphotericin B	[0.5]	ND		ND		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	[16]	ND		ND		
	Itraconazole	2	ND		ND		
	Posaconazole	0.25	ND		ND		
	Voriconazole	ND	ND		ND		
	Isavuconazole	ND	ND		ND		
<i>C. lusitanae</i>	Amphotericin B	[0.5]	ND		ND		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	ND	ND		ND		
	Itraconazole	0.125	ND		ND		
	Posaconazole	ND	ND		ND		
	Voriconazole	ND	ND		ND		
	Isavuconazole	ND	ND		ND		

Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.3 and E.Def 11.0 procedures

Version 2.0, valid from 2020-09-24

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
<i>S. cerevisiae</i>	Amphotericin B	[0.5]	ND			ND	
	Anidulafungin	ND	ND			ND	
	Micafungin	ND	ND			ND	
	Fluconazole	ND	ND			ND	
	Itraconazole	ND	ND			ND	
	Posaconazole	ND	ND			ND	
	Voriconazole	ND	ND			ND	
	Isavuconazole	ND	ND			ND	
<i>C. kefyr</i>	Amphotericin B	[1]	ND			ND	
	Anidulafungin	ND	ND			ND	
	Micafungin	ND	ND			ND	
	Fluconazole	[1]	ND			ND	
	Itraconazole	ND	ND			ND	
	Posaconazole	ND	ND			ND	
	Voriconazole	ND	ND			ND	
	Isavuconazole	ND	ND			ND	
<i>C. neoformans</i>	Amphotericin B	[1]	1			1	
	Flucytosine	ND	ND			ND	
	Anidulafungin	ND	ND			ND	
	Micafungin	ND	ND			ND	
	Fluconazole	ND	ND			ND	
	Itraconazole	ND	ND			ND	
	Posaconazole	0.5	ND			ND	
	Voriconazole	0.5	ND			ND	
Isavuconazole	ND	ND			ND		
<i>C. gattii</i>	Amphotericin B	[0.5]	ND			ND	
	Flucytosine	ND	ND			ND	
	Anidulafungin	ND	ND			ND	
	Micafungin	ND	ND			ND	
	Fluconazole	ND	ND			ND	
	Itraconazole	ND	ND			ND	
	Posaconazole	1	ND			ND	
	Voriconazole	ND	ND			ND	
Isavuconazole	ND	ND			ND		

Comments: \* ECOFFs indicated in brackets [] are tentative.

**Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.3 and E.Def 11.0 procedures**

Version 2.0, valid from 2020-09-24

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
<i>A. flavus</i>	Amphotericin B	4	-		-		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	ND	ND		ND		
	Itraconazole	1	1		1	2	Report as R with the comment that in some clinical situations (non-invasive infections) itraconazole can be used provided sufficient exposure is ensured.
	Posaconazole	0.5	ND		ND		
	Voriconazole	2	ND		ND		
	Isavuconazole	2	1	#	2	2	If voriconazole wild-type (voriconazole MIC ≤ 2 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 for <i>A. flavus</i> . Clinically documented isavuconazole resistance in absence of voriconazole resistance is extremely rare and mechanisms conferring isavuconazole monoresistance have not been described. 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 <sup>3</sup>
<i>A. fumigatus</i>	Amphotericin B	1	1		1		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	ND	ND		ND		
	Itraconazole	1	1		1	2	Report as R with the comment that in some clinical situations (non-invasive infections) itraconazole can be used provided sufficient exposure is ensured.
	Posaconazole	0.25	0.125	#	0.25	0.25	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 .

**Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.3 and E.Def 11.0 procedures**

Version 2.0, valid from 2020-09-24

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
<i>A. fumigatus</i>	Voriconazole	1	1		1	2	Report as R with the comment that in some clinical situations (non-invasive infections) voriconazole can be used provided sufficient exposure is ensured.
	Isavuconazole	2	1	#	2	2	If voriconazole S, report as isavuconazole S and add the following comment: The MIC of 2 mg/L is wild type but one dilution above the S breakpoint due to overlapping wt and non-wt populations.* Clinically documented isavuconazole resistance in absence of voriconazole resistance is extremely rare and mechanisms conferring isavuconazole monoresistance have not been described. See rationale documents for more information. If not S to voriconazole, report as isavuconazole R and refer to reference laboratory for CYP51A sequencing and confirmation of MICs*
<i>A. nidulans</i>	Amphotericin B	[4]**	-		-		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	ND	ND		ND		
	Itraconazole	1	1		1	2	Report as R with the comment that in some clinical situations (non-invasive infections) itraconazole can be used provided sufficient exposure is ensured.
	Posaconazole	0.5	ND		ND		
	Voriconazole	1	1		1	2	Report as R with the comment that in some clinical situations (non-invasive infections) voriconazole can be used provided sufficient exposure is ensured.
	Isavuconazole	0.25	0.25		0.25		
<i>A. niger</i>	Amphotericin B	[0.5]	1		1		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	ND	ND		ND		
	Itraconazole	4	ND		ND		
	Posaconazole	0.5	ND		ND		
	Voriconazole	2	ND		ND		
	Isavuconazole	4	ND		ND		

**Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.3 and E.Def 11.0 procedures**

Version 2.0, valid from 2020-09-24

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
<i>A. terreus</i>	Amphotericin B	8	-		-		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	ND	ND		ND		
	Itraconazole	0.5	1		1	2	Report as R with the comment that in some clinical situations (non-invasive infections) itraconazole can be used provided sufficient exposure is ensured.
	Posaconazole	0.25	0.125	#	0.25	0.25	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 <i>CYP51A</i> sequencing and confirmation of MICs.*
	Voriconazole	2	ND		ND		
	Isavuconazole	1	1		1		
<i>Fusarium (Gibberella) fujikuroi</i> SC	Amphotericin B	[8]	ND		ND		
<i>Fusarium solani</i> SC	Amphotericin B	[8]	ND		ND		

**Comments:** # means there is no "I" category as the MIC in between S and R represents only an ATU because this MIC corresponds to both wt and non-wt isolates (MIC is 1 dilution)



## Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.3 and E.Def 11.0 procedures

Version 2.0, valid from 2020-09-24

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
<i>T. interdigitale</i>	Amorolfin	[0.5] <sup>1</sup>	ND		ND		
	Amphotericin B	ND	ND		ND		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	ND	ND		ND		
	Isavuconazole	ND	ND		ND		
	Itraconazole	[0.25]	ND		ND		
	Posaconazole	ND	ND		ND		
	Terbinafine	[0.125]	ND		ND		
Voriconazole	[1]	ND		ND			
<i>T. rubrum</i>	Amorolfin	[0.125]	ND		ND		
	Amphotericin B	ND	ND		ND		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	ND	ND		ND		
	Isavuconazole	ND	ND		ND		
	Itraconazole	[(0.25)] <sup>2</sup>	ND		ND		
	Posaconazole	ND	ND		ND		
	Terbinafine	[0.03]	ND		ND		
Voriconazole	[0.125]	ND		ND			

### Comments:

<sup>1</sup> ECOFFs indicated in brackets [ ] are tentative.

<sup>2</sup> itraconazole MIC distributions were wider than normally, the tentative ECOFF is therefore associated with uncertainty and values presented in a parenthesis.