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

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 9.4 and E.Def 11.0 procedures

Version 3.0, valid from 2022-01-18

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 9.4 and E.Def 11.0 procedures. Version 3, 2022. http://www.eucast.org."

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 9.4 and E.Def 11.0 procedures

Version 3.0, valid from 2022-01-18

Version 3.0, valid from 2022-01-18	**Changes** Cells containing a change or an addition from document v.2.0 are marked yellow (Format changes are not marked yellow).
Yeasts	Itraconazole ECOFFs against *C. albicans, C. guilliermondii,* and *C. lusitaniae,* have been revised and an ECOFF against *Saccharomyces cerevisiae* established.
Moulds	Itraconazole ECOFFs against *A. nidulans, A. niger,* and *A. terreus* have been revised.
Dermatophytes	*T. interdigitale* changed to *T. indotinea,* and a footnote has been added concerning the itraconazole versus *T. rubrum* range.

Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.4 and E.Def 11.0 procedures

Version 3.0, valid from 2022-01-18

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
C. albicans	Amphotericin B	1	1		1		
	Anidulafungin	0.03	0.03		0.03		
	Micafungin	0.016	0.016		0.016	0.03	If S to anidulafungin, report as S and add the following comment: Isolates susceptible to anidulafungin with micafungin MIC of 0.03 mg/L do not harbour an *fks* mutation conferring resistance to the echinocandins. If not S to anidulafungin, report as R and refer to reference laboratory for *fks* sequencing and confirmation of MICs.
	Fluconazole	0.5	2	4	4		
	Itraconazole	0.03	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		
C. dubliniensis	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		
C. glabrata	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		
C. krusei	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 9.4 and E.Def 11.0 procedures

Version 3.0, valid from 2022-01-18

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
C. parapsilosis	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		
C. tropicalis	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		
C. guilliermondii	Amphotericin B	(0.5)	ND		ND		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	(16)	ND		ND		
	Itraconazole	(1)	ND		ND		
	Posaconazole	0.25	ND		ND		
	Voriconazole	ND	ND		ND		
	Isavuconazole	ND	ND		ND		
C. lusitaniae	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 9.4 and E.Def 11.0 procedures

Version 3.0, valid from 2022-01-18

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
S. cerevisiae	Amphotericin B	(0.5)	ND		ND		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	ND	ND		ND		
	Itraconazole	(2)	ND		ND		
	Posaconazole	ND	ND		ND		
	Voriconazole	ND	ND		ND		
	Isavuconazole	ND	ND		ND		
C. kefyr	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		
C. neoformans	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		
C. gattii	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 (TECOFF).
ND: Not determined.

Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.4 and E.Def 11.0 procedures

Version 3.0, valid from 2022-01-18

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
A. flavus	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 *A. flavus*. 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[3]
A. fumigatus	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 9.4 and E.Def 11.0 procedures

Version 3.0, valid from 2022-01-18

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
***A. fumigatus* cont.**	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*
A. nidulans	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		
A. niger	Amphotericin B	(0.5)	1		1		
	Anidulafungin	ND	ND		ND		
	Micafungin	ND	ND		ND		
	Fluconazole	ND	ND		ND		
	Itraconazole	2	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 9.4 and E.Def 11.0 procedures

Version 3.0, valid from 2022-01-18

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
A. terreus	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 *CYP51A* sequencing and confirmation of MICs.*
	Voriconazole	2	ND		ND		
	Isavuconazole	1	1		1		
***Fusarium* (*Gibberella*) *fujikuroi* SC**	Amphotericin B	(8)	ND		ND		
***Fusarium solani* 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 below the ECOFF), and shall be translated to S or R as described in the "Recommendation for ATU results" column.
ND: Not determined.
"-" 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.
* 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.
** ECOFFs indicated in brackets ( ) are tentative (TECOFF).

Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.3, E.Def 9.4 and E.Def 11.0 procedures

Version 3.0, valid from 2022-01-18

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
T. indotineae [2]	Amorolfin	(0.5)[1]	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)[2]	ND		ND		
	Posaconazole	ND	ND		ND		
	Terbinafine	(0.125)	ND		ND		
	Voriconazole	(1)	ND		ND		
T. rubrum	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)[2,3]	ND		ND		
	Posaconazole	ND	ND		ND		
	Terbinafine	(0.03)	ND		ND		
	Voriconazole	(0.125)	ND		ND		

Comments:

[1] ECOFFs indicated in brackets ( ) are tentative.

[2] TECOFFs against *T. indotineae* (formerly the Indian variant of *T. interdigitale*) and *T. rubrum* were determined based on a shared isolate collection tested in 10 laboratories as part of a recently published study (Multicentre validation of a EUCAST method for the antifungal susceptibility testing of microconidia-forming dermatophytes; J Antimicrob Chemother, 2020) and a comment supporting the name change (J Antimicrob Chemother, 2022).

[3] MIC distributions were wider than normally, the TECOFF is therefore associated with uncertainty. They apply to MICs determined using E.Def 11.0 and with 50% endpoint criteria.