Candida Inpatient Antibiogram for Nebraska Medical Center (2016-2018)

Isolates Included in Analysis

Candida species isolated from sterile sites (blood, cerebral spinal fluid, joint fluid, pleural fluid, and pericardial fluid) routinely undergo susceptibility testing per CLSI guidelines using the Sensititre YeastOne test (Trek Diagnostic Systems, Cleveland, Ohio) at the Nebraska Medical Center. Isolates from other sources may be tested at the request of the physician and are included in this analysis. *Candida* isolates tested from inpatients corresponding to first isolate per calendar year that underwent susceptibility testing during the period of Jan 1, 2016 until Dec 31, 2018 were evaluated. See **Table 1** for Antibiogram. Only those *Candida* spp. with ≥10 isolates tested in the evaluation period were included in the antibiogram. This deviates from the CLSI guideline of ≥30 isolates and those with less than 30 isolates should be used with caution. Epidemiological cutoff values (ECV) were used to determine resistance when interpretations were unavailable (see next section for more information).

Interpretations by CLSI guidelines

This antibiogram was created using the newest CLSI guideline (M60, Nov 2017). It should be noted these guidelines have undergone extensive revisions. Interpretations for general *Candida* spp. have been removed; this mainly affects the interpretations for less commonly isolated *Candida* spp. (e.g. *C. krusei*, *C. guilliermondii*, *C. dubliniensis* and *C. lusitaniae*). Interpretative information is no longer available for 5-flucytosine for any *Candida* spp. and is not included in this antibiogram. Importantly, the only antifungal with an interpretation of Susceptible-Dose Dependent (SDD) is now fluconazole (see Table 2B). Interpretations for posaconazole and itraconazole for all *Candida* spp. are no longer recognized; many of these have been replaced by the ECVs but vary by C*andida* spp. ECVs are MIC (minimum inhibitory concentration) values that separate populations of *Candida* into isolates with and without acquired or mutation-based resistance. For example, the ECV to amphotericin B is 2 µg/ml for *Candida glabrata*. This means that those isolates with an MIC value of ≤ 2 do not encode resistance determinants whereas those isolates with MIC values >2 are considered resistant to amphotericin B due to the acquisition of resistance determinants. ECV's do not account for clinical outcomes or PK/PD information used in interpretative values (susceptible/intermediate/resistance). ECV for *Candida* spp. are outlined in the CLSI guidance document M59. See Tables 2A, 2B, 2C for these new interpretations.

Table 1. Cumulative *Candida* spp. Antibiogram 2016-2018

Candida species	# of isolates	Anidulafungin	Caspofungin	Micafungin	Fluconazole	Posaconazole*	Voriconazole	Amphotericin B*
C. albicans/dubliniensis [&]	144	100	100	100	97.2	95.1	98.6	100
C. glabrata	117	96.6	97.4	95.7	89.7**	86.3	58.1*	100
C. krusei	10^	100	100	100	IR	100	100	100
C. parapsilosis complex	33	100	100	100	97	100	100	100
C. tropicalis	16^	100	100	100	81.3	62.5	75.0	100

* ECV values used to determine resistance (see Table 2C)

** fluconazole-susceptible *C. glabrata* isolates are all categorized as susceptible does dependent (SDD), no susceptible catergory exists

^ These *Candidia* spp. have less then the recommended isolates and should be interperated with caution

IR *C. krusei* is intrinsically resistant to fluconazole

[&] *C. albicans* and *C. dubliniensis* are grouped as *C. albicans/dubliniensis* due the inability to differentiate between these two species. *C. albicans* breakpoints used to determine susceptibility

Table 2A. Candida Breakpoints - Echinocandins

		2017 M60 MIC Breakpoints and Interpretive Categories, µg/ml				
Antifungal Agent	**Species**	**S**	**I**	**SDD**	**R**	**ECV (M59)**
Anidulafungin/ Caspofungin[&]	*C. albicans*	≤ 0.25	0.5	-	≥ 1	
	C. glabrata	≤ 0.12	0.25	-	≥ 0.5	
	C. guilliermondii	≤ 2	4	-	≥ 8	
	C. krusei	≤ 0.25	0.5	-	≥ 1	
	C. parapsilosis	≤ 2	4	-	≥ 8	
	C. tropicalis	≤ 0.25	0.5	-	≥ 1	
	C. dubliniensis			ECV		0.12[&]
	C. lusitaniae			ECV		1[&]
Micafungin	*C. albicans*	≤ 0.25	0.5	-	≥ 1	
	C. glabrata	≤ 0.06	0.12	-	≥ 0.25	
	C. guilliermondii	≤ 2	4	-	≥ 8	
	C. krusei	≤ 0.25	0.5	-	≥ 1	
	C. parapsilosis	≤ 2	4	-	≥ 8	
	C. tropicalis	≤ 0.25	0.5	-	≥ 1	
	C. dubliniensis			ECV		0.12
	C. lusitaniae			ECV		0.5

[&] Anidulafungin only

Table 2B. Candida Breakpoints - Azoles with Interpretations

		2017 M60 MIC Breakpoints and Interpretive Categories, µg/ml				
Antifungal Agent	**Species**	**S**	**I**	**SDD**	**R**	**ECV (M59)**
Fluconazole	*C. albicans*	≤ 2	-	4	≥ 8	
	C. glabrata	-	-	≤ 32	≥ 64	
	C. guilliermondii	ECV				8
	C. krusei			Intrinsic Resistance		
	C. parapsilosis	≤ 2	-	4	≥ 8	
	C. tropicalis	≤ 2	-	4	≥ 8	
	C. dubliniensis	ECV				0.5
	C. lusitaniae	ECV				1
Voriconazole	*C. albicans*	≤ 0.12	0.25-0.5	-	≥ 1	
	C. glabrata			ECV		0.25
	C. guilliermondii			insufficient data		
	C. krusei	≤ 0.5	1	-	≥ 2	
	C. parapsilosis	≤ 0.12	0.25-0.5	-	≥ 1	
	C. tropicalis	≤ 0.12	0.25-0.5	-	≥ 1	
	C. dubliniensis			insufficient data		
	C. lusitaniae			insufficient data		

Table 2C. Candida Breakpoints - Antifungals without Interpretations

		2017 M60 MIC Breakpoints and Interpretive Categories, µg/ml				
Antifungal Agent	**Species**	**S**	**I**	**SDD**	**R**	**ECV (M59)**
Amphotericin B	*C. albicans*			ECV		2
	C. glabrata			ECV		2
	C. guilliermondii			insufficient data		
	C. krusei			ECV		2
	C. parapsilosis			ECV		2
	C. tropicalis			ECV		2
	C. dubliniensis			insufficient data		
	C. lusitaniae			insufficient data		
5-Flucytosine	*All Candidia sp.*			insufficient data		
Itraconazole	*C. albicans*			insufficient data		
	C. glabrata			ECV		4
	C. guilliermondii			insufficient data		
	C. krusei			ECV		1
	C. parapsilosis			insufficient data		
	C. tropicalis			ECV		0.5
	C. dubliniensis			insufficient data		
	C. lusitaniae			ECV		1
Posaconazole	*C. albicans*			ECV		0.06
	C. glabrata			ECV		1
	C. guilliermondii			ECV		0.5
	C. krusei			ECV		0.5
	C. parapsilosis			ECV		0.25
	C. tropicalis			ECV		0.12
	C. dubliniensis			insufficient data		
	C. lusitaniae			ECV		0.06
Isavuconazole	All *Candidia spp.*			insufficient data		

References

1. CLSI. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts, 4th Edition*. CLSI standard M27. Wayne, PA: Clinical and Laboratory Standards Institute; 2017.
2. CLSI. *Performance Standards for Antifungal Susceptibility Testing in Yeasts*, 1st Edition. CLSI supplement M60. Wayne, PA: Clinical and Laboratory Standards Institute; 2017.
3. CLSI. *Principles and Procedures for the Development of Epidemiological Cutoff Values for Antifungal Susceptibility Testing*, 1st Edition. CLSI guideline M57. Wayne, PA: Clinical and Laboratory Standards Institute; 2016.
4. CLSI. *Epidemiological Cutoff Values for Antifungal Susceptibility Testing*, 2nd Edition. CLSI guideline M59. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.

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