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Nationales Antibiotika-
Sensitivitätstest-Komitee

Neues von EUCAST

Sören Gatermann
Ruhr-Universität Bochum
Vorsitzender des NAK
Chairman des EUCAST

EUCAST European Committee on Antimicrobial Susceptibility Testing

Anmerkungen

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7. Unless otherwise stated, breakpoints are valid for all indications. For information on species and agents for endocarditis, see https://www.eucast.org/eucastguidancedocuments/.

19. Definitions of "uncomplicated UTI" and “Infections originating from the urinary tract” used with EUCAST breakpoints:
Uncomplicated UTI: Acute, sporadic or recurrent lower urinary tract infections (uncomplicated cystitis) in patients with no known relevant anatomical or functional abnormalities within the urinary tract or comorbidities.
Infections originating from the urinary tract: Infections originating from, but not confined to, the urinary tract, including acute pyelonephritis and bloodstream infections, except severe sepsis. For oral agents, the breakpoints mainly apply to non-severe infections and oral step-down therapy.

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Unter der Dosierungstabelle

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Trimethoprim	None	None	0.16 g x 2 oral	
Trimethoprim-sulfamethoxazole	(0.16 g trimethoprim + 0.8 g sulfamethoxazole) x 2 oral or (0.16 g trimethoprim + 0.8 g sulfamethoxazole) x 2 iv	(0.24 g trimethoprim + 1.2 g sulfamethoxazole) x 2 oral or (0.24 g trimethoprim + 1.2 g sulfamethoxazole) x 2 iv	(0.16 g trimethoprim + 0.8 g sulfamethoxazole) x 2 oral	**Meningitis**: (5 mg/kg up to 0.48 g trimethoprim + 25 mg/kg up to 2.4 g sulfamethoxazole) x 3 iv

** cSSTI = complicated skin and skin structure infection

Information on EUCAST breakpoints and dosing for challenging infection sites and on special situations for antimicrobial treatment EUCAST breakpoints are based on standard and, if applicable, high exposure to antimicrobial agents. The dosing regimens are either those listed in the Summary of Product Characteristics approved by EMA (European Medicines Agency) or, especially with older agents, doses that are commonly administered in European countries. For some more common infections or when the usual severity of the infection requires special attention, EUCAST has produced additional dosing guidance (e.g. urinary tract infections) and/or breakpoints (e.g. meningitis).There are other sites and infections where the antibiotic exposure of the organism may be impaired and where therapy may require higher dosing or a change in the mode of administration to ensure the desired exposure. Such situations include, but are not limited to, endocarditis, bone and joint infections, and abscesses in the central nervous system.Since EUCAST is a breakpoint committee it will not give dosing or other treatment recommendations for such conditions, but will list specific breakpoints for challenging infections when applicable. Refer to textbooks or national/international treatment guidelines for more information on dosing regimens in challenging infections. In addition to these clinical situations, rare resistance mechanisms may require tailored or unusual therapeutic approaches and often these therapies are still discussed in the community. Examples include borderline resistant S. aureus (BORSA), vancomycin-variable enterococci and A. baumannii producing KPC. For such isolates, EUCAST currently does not give specific recommendations, neither for testing nor for selection of the appropriate antimicrobial agent.

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Enterobacterales Aminopenicilline

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Penicillins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			N N L
	S ≤	R >	ATU		S ≥	R <	ATU	
Benzylpenicillin	-	-			-	-		1
Amoxicillin oral (uncomplicated UTI only)[1]	8	8		-	Note[B]	Note[B]		
Amoxicillin oral (other indications)[1]	(0.001)[3]	(8)[3]		-	Note[D,E]	Note[D,E]		
Amoxicillin-clavulanic acid iv[1]	8[4]	8[4]		20-10	19[A]	19[A]	19-20	
Amoxicillin-clavulanic acid oral (infections originating from the urinary tract)[1]	0.001[4]	8[4]		20-10	50[A]	19[A]	19-20	
Amoxicillin-clavulanic acid oral (uncomplicated UTI only)[1]	32[4]	32[4]		20-10	16[A]	16[A]		
Amoxicillin-clavulanic acid oral (other indications)[1]	(0.001)[3,4]	(8)[3,4]		20-10	(50)[A,D]	(19)[A,D]	19-20	

Angabe also als (I)

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Stenotrophomonas maltophilia

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	S ≤	R >	ATU	(µg)	S ≥	R <	ATU	**Lettered notes relate to the disk diffusion method.**
Ceftazidime	-	-			-	-		**1.** Broth microdilution MIC determination must be performed in iron-depleted Mueller-Hinton broth and specific reading instructions must be followed. For testing conditions and reading instructions, see https://www.eucast.org/eucastguidancedocuments/. **2/A.** The *in vitro* activity of cefiderocol against *Stenotrophomonas maltophilia* is comparable to the activity of the agent against *Enterobacterales* and there is also animal data to suggest efficacy. However, there is insufficient clinical data to determine a clinical breakpoint. Isolates with MIC values ≤0.5 mg/L (zone diameter ≥28 mm) are mostly devoid of resistance mechanisms. Isolates with MICs 1-2 mg/L have acquired resistance mechanisms which may result in impaired clinical response. Isolates with MIC values >2 mg/L (zone diameter <22 mm) will likely be resistant.
Cefepime	-	-			-	-		
Cefiderocol[1]	Note[2]	Note[2]		30	Note[A]	Note[A]		

Monobactams	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes **Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.**
	S ≤	R >	ATU		S ≥	R <	ATU	
Aztreonam	-	-			-	-		
Aztreonam-avibactam	IE	IE			IE	IE		

Fluoroquinolones	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes **Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.**
	S ≤	R >	ATU		S ≥	R <	ATU	
Ciprofloxacin	Note[1]	Note[1]			Note[A]	Note[A]		**1. Fluoroquinolones have been used in combination therapy. The ECOFF can be used to exclude acquired resistance mechanisms.** **A. Disk diffusion criteria are not available.**
Levofloxacin	Note[1]	Note[1]			Note[A]	Note[A]		

Tetracyclines	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes **Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.**
	S ≤	R >	ATU		S ≥	R <	ATU	
Minocycline	Note[1,2]	Note[1,2]			Note[A]	Note[A]		**1.** Tetracyclines have been used in combination therapy. The ECOFF can be used to exclude acquired resistance mechanisms. **2.** Pertains to intravenous therapy. Oral therapy will lead to insufficient exposure. **A.** Disk diffusion criteria are not available.
Tigecycline	Note[1]	Note[1]			Note[A]	Note[A]		

Miscellaneous agents	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes **Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.**
	S ≤	R >	ATU		S ≥	R <	ATU	
Trimethoprim-sulfamethoxazole[1]	0.001	2		1.25-23.75	50[A]	16[A,B]		**1. Trimethoprim:sulfamethoxazole in the ratio 1:19. Breakpoints are expressed as the trimethoprim concentration.** **A. There may be growth within the inhibition zone. The density of growth may vary from a fine haze to substantial growth (see pictures below). If any zone edge can be seen, ignore growth within the inhibition zone and read the zone diameter.** **B. Trimethoprim-sulfamethoxazole resistance in *S. maltophilia* is rare and should be**

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Stenotrophomonas maltophilia

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Cephalosporins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU		S ≥	R <	ATU	**Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.**
Ceftazidime	-	-			-	-		**1.** Broth microdilution MIC determination must be performed in iron-depleted Mueller-Hinton broth and specific reading instructions must be followed. For testing conditions and reading instructions, see https://www.eucast.org/eucastguidancedocuments/.
Cefepime	-	-			-	-		
Cefiderocol[1]	Note[2]	Note[2]		30	Note[A]	Note[A]		**2/A.** The *in vitro* activity of cefiderocol against *Stenotrophomonas maltophilia* is comparable to the activity of the agent against *Enterobacterales* and there is also animal data to suggest efficacy. However, there is insufficient clinical data to determine a clinical breakpoint. Isolates with MIC values ≤0.5 mg/L (zone diameter ≥28 mm) are mostly devoid of resistance mechanisms. Isolates with MICs 1-2 mg/L have acquired resistance mechanisms which may result in impaired clinical response. Isolates with MIC values >2 mg/L (zone diameter <22 mm) will likely be resistant.

Cefiderocol

≥ 28mm	wahrscheinlich wildtypisches Isolat, Cefiderocol möglicherweise geeignet für die Therapie
22-27 mm	wahrscheinlich erworbene Resistenz, Bedeutung für klinischen Effekt unklar
< 22 mm	sehr wahrscheinlich resistent

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Stenotrophomonas maltophilia

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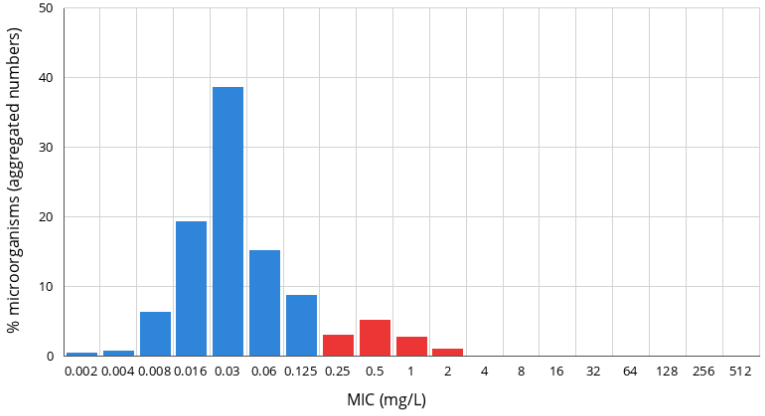
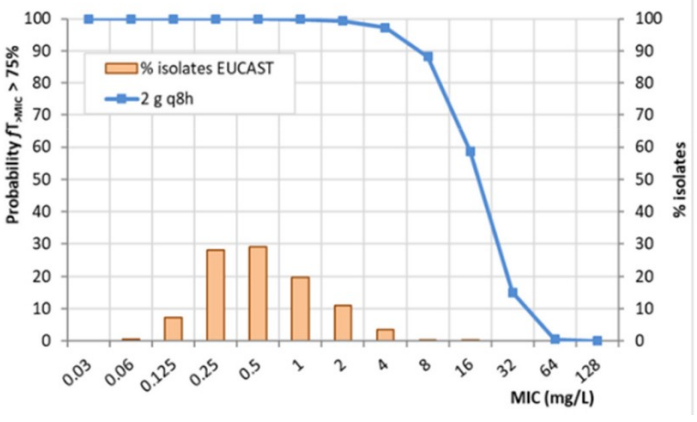
ECOFF bei 0,125



PTA bei 95% bis MHK 4



Barassa Antibiotics 13:553;2024

Tierexperimente mit Stämmen mit MHK 0.06-0.5 mg/L durchgehend bessere Ergebnisse als Vergleichssubstanzen (Chen 2019, Nakamura 2021).

Humane Daten fast ausschließlich mit Isolaten mit MHK ≤ 0,25 mg/L, nur ein Fall mit 1 mg/L (Versagen). In verschiedenen Kombinationen angewendet.

Auf ≤ 0,5 mg/L lässt sich mit einem Disktest untersuchen (≥ 28 mm)

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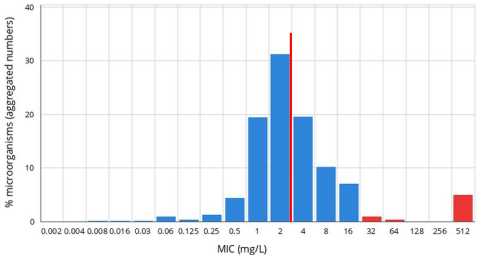
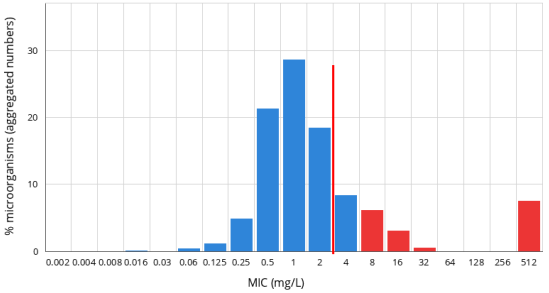
- Fluorochinolone (Ciprofloxacin, Levofloxacin)
- Tetracycline (Minocyclin, Tigecyclin)
- Kombinationen scheinen nicht besser zu sein als Monotherapien

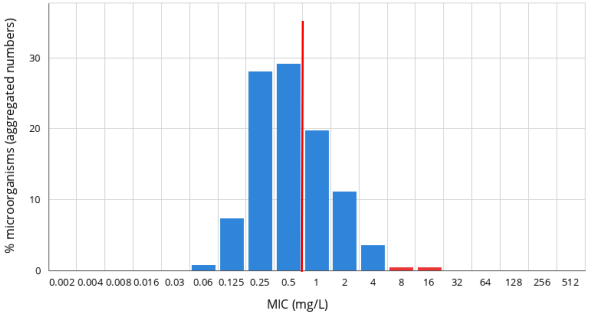
Ciprofloxacin



Levofloxacin



Tigecyclin



Maximale Grenzwerte (—) immer in der Verteilung, somit „ungeeignet“
Minocyclin in der i.v.-Version empfohlen, in Europa nicht verfügbar
Kein Disk-Test möglich
MHK-Bestimmung und ECOFF als Orientierung

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Stenotrophomonas maltophilia

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Guidance Document on *Stenotrophomonas maltophilia*

Version 2, November 2024

The organism

Stenotrophomonas maltophilia is a ubiquitous environmental organism. In patients, it is most often associated with colonisation, but is an occasional cause of infection, particularly in immunocompromised patients and patients with cystic fibrosis [1-3]. Most commonly *S. maltophilia* is recovered from lower respiratory tract samples, in patients who are colonised or infected.

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Acinetobacter spp.

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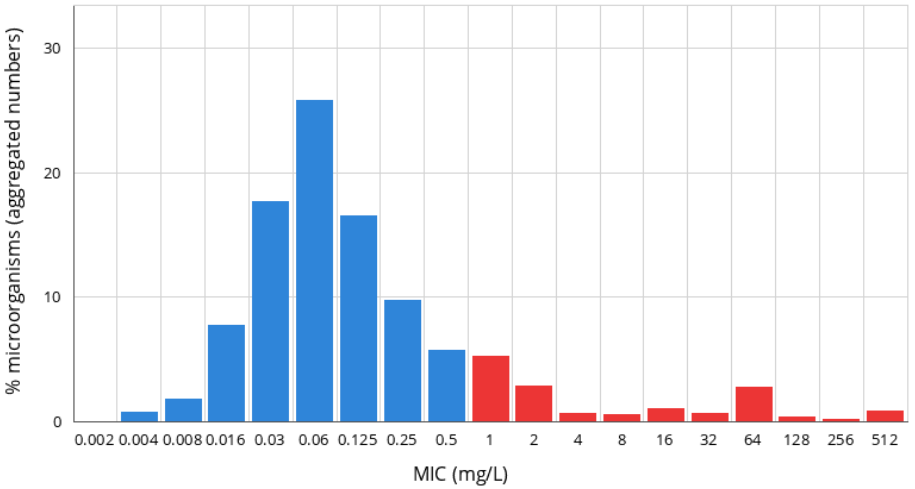

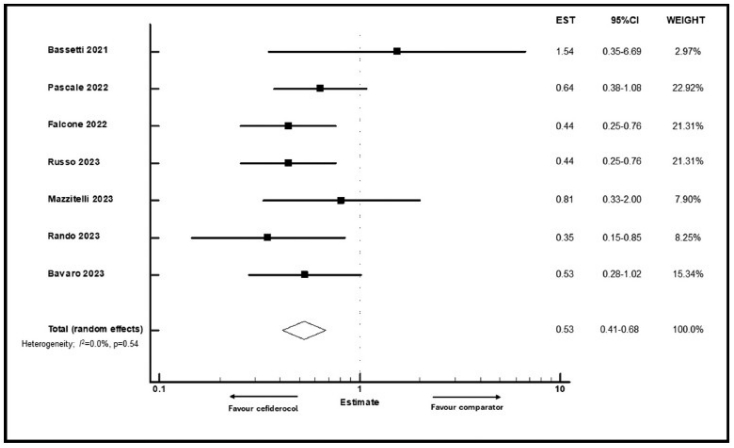

Figure 1. Updated forest plot of mortality rate in patients treated with cefiderocol-based regimens vs. non-cefiderocol-based regimens for CRAB infections.

Onorato et al 2024, meist keine MHK-Daten, die wenigen waren unter 1mg/L

≥ 21 mm	wahrscheinlich wildtypisches Isolat, Cefiderocol möglicherweise geeignet für die Therapie
17 – 20 mm	wohl erworbene Resistenzmechanismen
< 17 mm	MHK > 2, höchstwahrscheinlich resistent

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Enterokokken

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- Grenzwerte nun für (fast) alle Enterokokkenspezies gültig
- dadurch einige Änderungen,
  - *E. casseliflavus* und *E. gallinarum* Vancomycin ‚-‘
  - Anpassung der Grenzwerte für
    - Tigecyclin
    - Eravacyclin

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Enterokokken

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Penicillins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			No Nu Le
	S ≤	R >	ATU		S ≥	R <	ATU	
Benzylpenicillin	-	-			-	-		1/
Ampicillin iv	4	4		2	10[A]	10[A]		2. pr
Ampicillin-sulbactam iv[2]	Note[1]	Note[1]			Note[B]	Note[B]		3/
Amoxicillin iv	4[1]	4[1]			Note[B]	Note[B]		m
Amoxicillin oral (uncomplicated UTI only)	4[1]	4[1]			Note[B]	Note[B]		(s 4/
Amoxicillin oral (other indications), *E. faecalis*	(0.001)[3,4]	(4)[3,4]			Note[C,D]	Note[C,D]		eu 5.
Amoxicillin-clavulanic acid iv[2]	Note[1]	Note[1]			Note[B]	Note[B]		A.
Amoxicillin-clavulanic acid oral[2] (uncomplicated UTI only)	Note[1]	Note[1]			Note[B]	Note[B]		
Amoxicillin-clavulanic acid oral[2] (other indications), *E. faecalis*	Note[3,4]	Note[3,4]			Note[C,D]	Note[C,D]		
Piperacillin, *E. faecalis*	0.001	16		30	50	18		
Piperacillin-tazobactam[2], *E. faecalis*	0.001[5]	16[5]		30-6	50	18		

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hämolysierende Streptokokken

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Penicillins[1]	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			No N Le
	S ≤	R >	ATU		S ≥	R <	ATU	
Benzylpenicillin[2], Streptococcus groups A, C and G	0.03	0.03		1 unit	23	23		1/A be ph in 2.
Benzylpenicillin[2], *S. agalactiae* (group B streptococci)	0.125	0.125		1 unit	18	18		

- Die Grenzwerte sind die ECOFFs, d.h., jedes Isolat mit höherer MHK oder kleinerem Hemmhof, ist ungewöhnlich.

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S. pneumoniae

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Penicillins[1]	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			N M L
	S ≤	R >	ATU		S ≥	R <	ATU	
Benzylpenicillin (indications other than endocarditis and meningitis)	0.06	1		1 unit[A]	Note[A,B]	Note[A,B]		1 u
Benzylpenicillin (endocarditis and meningitis)	0.06	0.06			Note[B]	Note[B]		(a
Ampicillin (indications other than endocarditis and meningitis)	0.5	1						
Ampicillin iv (endocarditis and meningitis)	0.5	0.5						2
Ampicillin-sulbactam[2]	Note[1,3]	Note[1,3]			Note[B,C]	Note[B,C]		3 n
Amoxicillin iv (indications other than endocarditis and meningitis)	Note[1,3]	Note[1,3]			Note[B,C]	Note[B,C]		4 L
Amoxicillin iv (endocarditis and meningitis)	0.5	0.5			Note[B]	Note[B]		A

Konsequent auch in Dosierungstabelle
Änderung der Penicillindosen nach MHK bei Pneumonie

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S. pneumoniae

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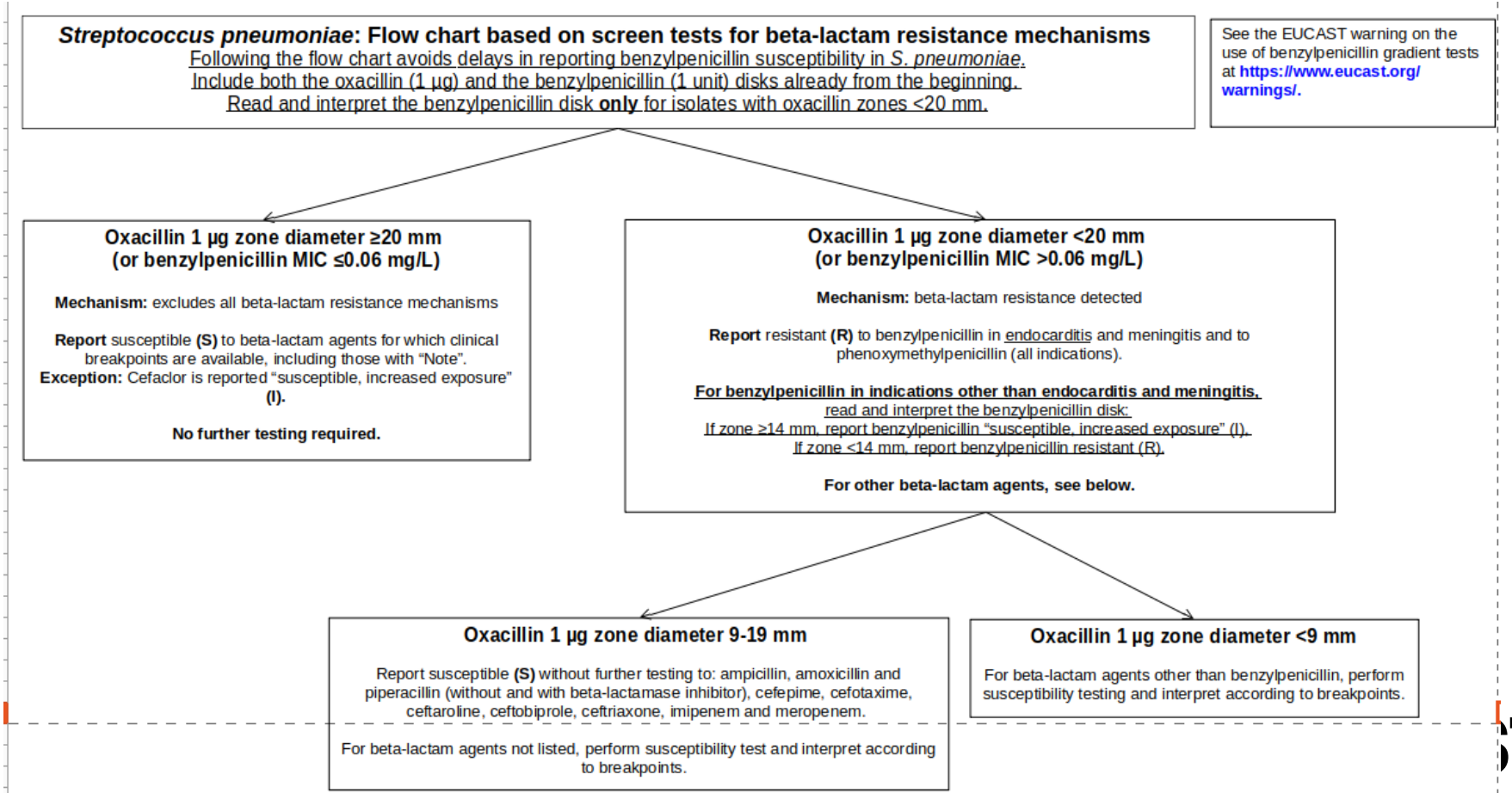

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Vergrünende Streptokokken

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Penicillins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			N N L
	S ≤	R >	ATU		S ≥	R <	ATU	
Benzylpenicillin (screen only)	0.25[1]	0.25[1]		1 unit	21[A]	21[A]		1, gr ag sc 2, er 3. 4, ar D (e
Benzylpenicillin (indications other than endocarditis)	0.25	1		1 unit	21	12		
Benzylpenicillin (endocarditis)	0.25	0.25			21	21		
Benzylpenicillin (endocarditis, in combination with other antimicrobial treatment)	(1)[2]	(1)[2]			(12)[B]	(12)[B]		
Ampicillin (indications other than endocarditis)	0.5	2		2	21	15		
Ampicillin iv (endocarditis)	0.5	0.5		2	21	21		
Ampicillin-sulbactam[3]	Note[1,4]	Note[1,4]			Note[A,C]	Note[A,C]		
Amoxicillin (indications other than endocarditis)	0.5	2			Note[A,C]	Note[A,C]		
Amoxicillin iv (endocarditis)	0.5	0.5			Note[A,D]	Note[A,D]		
Amoxicillin-clavulanic acid[3]	Note[1,4]	Note[1,4]			Note[A,C]	Note[A,C]		

Auch bei Endokarditis ist der Disk-Test ausreichend!

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Endokarditis Guidance-Dokument

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EUCAST guidance document on Infective Endocarditis:

Reporting of antimicrobial susceptibility testing results

December 2024

Background

Infective endocarditis is a severe condition requiring standardised and multidisciplinary management both for diagnosis and treatment. Correct targeted treatment is crucial to

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Endokarditis Besonderheiten

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- *S. pneumoniae*
- *H. influenzae*

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A. xylosoxidans

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Cefiderocol

≥ 26 mm	wahrscheinlich wildtypisches Isolat, Cefiderocol möglicherweise geeignet für die Therapie
22 – 25 mm	wohl erworbene Resistenzmechanismen
< 22 mm	MHK > 2, höchstwahrscheinlich resistent

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