

# EUCAST 2025

## Neuigkeiten

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# EUCAST Clinical Breakpoints v. 15.0

## European Committee on Antimicrobial Susceptibility Testing

Breakpoint tables for interpretation of MICs and zone diameters

Version 15.0, valid from 2025-01-01

### – General: Anwendbarkeit der BP (Breakpoints)

- Link to guidance documents added at the top of each table.
- Unless otherwise stated, breakpoints are valid also for special situations such as endocarditis and meningitis for relevant species and agents. Breakpoints for endocarditis and meningitis are listed on separate lines only when they differ from the general breakpoints. For information on species and agents for endocarditis, see <https://www.eucast.org/eucastguidancedocuments/>.
- Specific comments on endocarditis and meningitis in the flow charts for screening for beta-lactam resistance in *S. pneumoniae* and *H. influenzae* are only kept if the recommendations are not covered by the general recommendations.

### – Notes:

- Klarstellung Umgang mit PK/PD, Bedeutung IE

2. The use and limitations of PK/PD cut-off values in breakpoint setting are described separately in the tab "PK/PD cut-off values".

9. "IE" indicates that there is insufficient evidence that the organism or group is a good target for therapy with the agent. In these situations, follow the guidance in "When there are no breakpoints" (<https://www.eucast.org/eucastguidancedocuments/>).

- Hinweis auf Guidance Dokument Endokarditis
- Anpassung und Klarstellung „Infections originating from the urinary tract“

**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.

# Dosages used to define breakpoints

**EUCAST breakpoints are based on the following dosages. Alternative dosing regimens may result in equivalent exposure. The table should not be used as a guidance for dosing in clinical practice as dosages can vary widely by indication. It does not replace specific national, regional or local dosing guidelines. However, if national practices significantly differ from those listed below, EUCAST breakpoints may not be valid. Situations where less antibiotic is given as standard or high dose should be discussed locally or regionally. Information on EUCAST breakpoints and dosing for challenging infection sites and on special situations for antimicrobial treatment is available below the dosages table.**

## **Information on EUCAST breakpoints and dosing for challenging infection sites and on special situations for antimicrobial treatment**

1. 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).
2. 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.
3. 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.
4. 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.



# Dosages used to define breakpoints

- Neue Hinweise bei Benzylpenicillin

Penicillins	Standard dosage	High dosage	Uncomplicated UTI	Special situations
Benzylpenicillin	0.6 g (1 MU) x 4 iv	1.2 g (2 MU) x 6 iv		<p>Meningitis: 2.4 g (4 MU) x 6 iv</p> <p>Meningitis caused by <i>S. pneumoniae</i>: For a dose of 2.4 g (4 MU) x 6 iv, isolates with MIC <math>\leq</math> 0.06 mg/L are susceptible</p> <p>Pneumonia caused by <i>S. pneumoniae</i>: breakpoints are related to dosage: For a dose of 1.2 g (2 MU) x 4 iv, isolates with MIC <math>\leq</math> 0.5 mg/L are susceptible. For a dose of 2.4 (4 MU) g x 4 iv or 1.2 g (2 MU) x 6 iv, isolates with MIC <math>\leq</math> 1 mg/L are susceptible. For a dose of 2.4 g (4 MU) x 6 iv, isolates with MIC <math>\leq</math> 2 mg/L are susceptible.</p>

- Cephalosporine bei *S. aureus*
- Neue Dosierungen von
  - Cefepime-Enmetazobactam
  - Aztreonam-Avibactam

# Neue Substanzen

## Aztreonam-Avibactam

- Avibactam (Diazabicyclooctan-Nicht- $\beta$ -Lactam- $\beta$ -Lactamase-Inhibitor) in Kombination mit Aztreonam, Handelsname: Emblaveo<sup>®</sup>
- Behandlung von Infektionen durch aerobe gramnegative Organismen bei Erwachsenen mit eingeschränkten Behandlungsmöglichkeiten
  - Komplizierter Harnwegsinfekt
  - Komplizierte intraabdominelle Infektion
  - Nosokomial erworbene Pneumonie

Monobactams	Standard dosage	High dosage	Uncomplicated UTI	Special situations
Aztreonam	1 g x 3 iv	2 g x 4 iv		Severe <i>P. aeruginosa</i> infections: 2 g x 4 with extended 3-hour infusion
Aztreonam-avibactam	(2 g aztreonam + 0.67 g avibactam) x 1 followed by (1.5 g aztreonam + 0.5 g avibactam) x 4 iv over 3 hours			

# EUCAST

## Clinical Breakpoints v. 15.0

### – *Enterobacterales*:

- Amoxicillin oral (andere Indikationen): ( $S \leq 0,001$  mg/L) und ( $R > 8$  mg/L), keine PD BP

**E. Isolates susceptible to ampicillin are without phenotypically detectable resistance mechanisms and "amoxicillin oral (other indications)" can be used in high exposure in combination therapy (see Note 3/D). Isolates resistant to ampicillin can be reported resistant.**

- Amoxicillin-Clavulansäure oral (andere Indikationen) BP (50/19 mm; 0,001/8 mg/L)
- Cefepim-Enmetazobactam: BP (22/22 mm; 4/4 mg/L), ATU 21-22
- Ceftriaxone: Meningitis BP 27/27 mm, andere Indikationen BP 27/24 mm
- Aztreonam-Avibactam: BP (25/25 mm; 4/4 mg/L), ATU 22-24
- Azithromycin: neue Ablesehilfe

**B. When reading azithromycin zone diameters, take growth appearing as a thin inner zone on some batches of Mueller-Hinton agar into account.**

# EUCAST Clinical Breakpoints v. 15.0

Penicillins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU		S ≥	R <	ATU	
<b>Benzylpenicillin</b>	-	-		-	-			<p>Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.</p> <p>1. For information on how to implement the new aminopenicillin breakpoints, see <a href="https://www.eucast.org/eucastguidancedocuments/">https://www.eucast.org/eucastguidancedocuments/</a>.</p> <p>2. For susceptibility testing purposes, the concentration of sulbactam is fixed at 4 mg/L.</p> <p>3/D. For information on how to use breakpoints in brackets, see <a href="https://www.eucast.org/eucastguidancedocuments/">https://www.eucast.org/eucastguidancedocuments/</a>.</p> <p>4. For susceptibility testing purposes, the concentration of clavulanic acid is fixed at 2 mg/L.</p> <p>5. For susceptibility testing purposes, the concentration of tazobactam is fixed at 4 mg/L.</p> <p>6. Agar dilution is the reference method for mecillinam MIC determination.</p> <p>A. Ignore growth that may appear as a thin inner zone on some batches of Mueller-Hinton agars.</p> <p>B. Susceptibility inferred from ampicillin (iv or oral).</p> <p>C. Isolates susceptible to ampicillin (iv or oral) can be reported "susceptible, increased exposure" (I) to "amoxicillin oral (infections originating from the urinary tract)". Isolates resistant to ampicillin (iv or oral) can be reported resistant to "amoxicillin oral (infections originating from the urinary tract)".</p> <p>E. Isolates susceptible to ampicillin are without phenotypically detectable resistance mechanisms and "amoxicillin oral (other indications)" can be used in high exposure in combination therapy (see Note 3/D). Isolates resistant to ampicillin can be reported resistant.</p> <p>F. Ignore isolated colonies within the inhibition zone.</p>
Ampicillin iv <sup>1</sup>	8	8		10	14 <sup>A</sup>	14 <sup>A</sup>		
Ampicillin oral (uncomplicated UTI only) <sup>1</sup>	8	8		10	14 <sup>A</sup>	14 <sup>A</sup>		
Ampicillin-sulbactam iv <sup>1</sup>	8 <sup>2</sup>	8 <sup>2</sup>		10-10	14 <sup>A</sup>	14 <sup>A</sup>		
Ampicillin-sulbactam oral (uncomplicated UTI only) <sup>1</sup>	8 <sup>2</sup>	8 <sup>2</sup>		10-10	14 <sup>A</sup>	14 <sup>A</sup>		
Amoxicillin iv <sup>1</sup>	8	8		-	Note <sup>B</sup>	Note <sup>B</sup>		
Amoxicillin oral (infections originating from the urinary tract) <sup>1</sup>	0.001	8		-	Note <sup>C</sup>	Note <sup>C</sup>		
Amoxicillin oral (uncomplicated UTI only) <sup>1</sup>	8	8		-	Note <sup>B</sup>	Note <sup>B</sup>		
Amoxicillin oral (other indications) <sup>1</sup>	(0.001) <sup>3</sup>	(8) <sup>3</sup>		-	Note <sup>D,E</sup>	Note <sup>D,E</sup>		
Amoxicillin-clavulanic acid iv <sup>1</sup>	8 <sup>4</sup>	8 <sup>4</sup>		20-10	19 <sup>A</sup>	19 <sup>A</sup>	19-20	
Amoxicillin-clavulanic acid oral (infections originating from the urinary tract) <sup>1</sup>	0.001 <sup>4</sup>	8 <sup>4</sup>		20-10	50 <sup>A</sup>	19 <sup>A</sup>	19-20	
Amoxicillin-clavulanic acid oral (uncomplicated UTI only) <sup>1</sup>	32 <sup>4</sup>	32 <sup>4</sup>		20-10	16 <sup>A</sup>	16 <sup>A</sup>		
Amoxicillin-clavulanic acid oral (other indications) <sup>1</sup>	(0.001) <sup>3,4</sup>	(8) <sup>3,4</sup>		20-10	(50) <sup>A,D</sup>	(19) <sup>A,D</sup>	19-20	
Piperacillin	8	8		30	20	20		
Piperacillin-tazobactam	8 <sup>5</sup>	8 <sup>5</sup>	16	30-6	20	20	19	
Ticarcillin-clavulanic acid	8 <sup>6</sup>	16 <sup>4</sup>		75-10	23	20		
Temocillin (infections originating from the urinary tract), <i>E. coli</i> , <i>Klebsiella</i> spp. (except <i>K. aerogenes</i> ) and <i>P. mirabilis</i>	0.001	16		30	50 <sup>F</sup>	17 <sup>F</sup>		
Phenoxyethylpenicillin	-	-		-	-	-		
Oxacillin	-	-		-	-	-		
Cloxacillin	-	-		-	-	-		
Dicloxacillin	-	-		-	-	-		
Flucloxacillin	-	-		-	-	-		
Mecillinam oral (pivmecillinam) (uncomplicated UTI only), <i>E. coli</i> , <i>Citrobacter</i> spp., <i>Klebsiella</i> spp., <i>Raoultella</i> spp., <i>Enterobacter</i> spp. and <i>P. mirabilis</i>	8 <sup>5</sup>	8 <sup>5</sup>		10	15 <sup>F</sup>	15 <sup>F</sup>		



# Colistintestung

28.02.2025

## **Colistin gradient tests and disks have no place in susceptibility testing**

For many years EUCAST has **warned** users that colistin disk diffusion and gradient tests (Etest™ from bioMérieux and MTS™ from Liofilchem) fail to predict colistin resistance in all relevant bacteria.

**bioMérieux** has now (2025) informed EUCAST that they have stopped the production and all sales of colistin Etest.

**Liofilchem** on the other hand still produces colistin MTS™, but have since more than a year, removed the IVD label and introduced an RoU (Research Only) label which means it should not be used in clinical laboratories for predicting colistin susceptibility and resistance in bacteria.

So, whatever use there is for colistin gradient tests, it is certainly not related to clinical microbiology. Likewise, colistin disks have no place in disk diffusion susceptibility testing.

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# EUCAST

## Clinical Breakpoints v. 15.0

- *Pseudomonas spp.*
  - Cefepim: neue ATU 19-23 mm
  - Cefepim-Enmetazobactam: keine BP, da Ableitung von Cefepim
- *Acinetobacter spp.*
  - Cefiderocol: Neuer Hinweis, wie Isolate anhand der AST Ergebnisse (auch Plättchendiffusion) interpretiert werden können:

2IA. The *in vitro* activity of cefiderocol against *Acinetobacter spp.* 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  $\leq 0.5$  mg/L (zone diameter  $\geq 21$  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  $< 17$  mm) will likely be resistant.

Cefiderocol: Kein Hinweis auf erworbene Resistenz: mögliche Therapieoption.“

Cefiderocol: Hinweis auf erworbene Resistenz: Therapieoption mit möglichem verminderten klinischen Ansprechen.

Cefiderocol: Hinweis auf erworbene Resistenz: keine Therapieoption.“

# Cefiderocol

## – Weiterhin WARNUNG gültig:

- kommerzielle Gradientendiffusionstest und andere BMD Tests weiterhin problematisch  
**Blättchendiffusion empfohlen**
- Vorsicht bei der Wahl bestimmter Agarmedien und Discs

## – Analoge Vorgehensweise bei

- *Achromobacter xylosoxidans*
- *Stenotrophomonas maltophilia*

- Disk diffusion. Laboratories are recommended to start testing cefiderocol with disk diffusion. Resistance to beta-lactam agents is increasing and therapeutic alternatives are few. Disk diffusion, when correctly performed and calibrated using quality material and recommended quality control guidelines, is predictive of susceptibility and resistance outside the ATU.  
**Template zone diameter distributions for relevant species against which to calibrate in-ho**
- Inside the ATU, and as long as there is no alternative method to resolve interpretative uncertainties (eg MIC-testing in the routine laboratory or assistance from a reference laboratory), EUCAST recommends colleagues to ignore the ATU and interpret using the zone diameter breakpoints in the breakpoint table.
- However, as with all AST methods and for all antimicrobial agents, results depend on the quality of materials used. EUCAST does not have the resources to systematically investigate all products from all manufacturers. Below a few commonly used manufacturers of disks and MH agars are mentioned but others are not. Assume that those that are not mentioned may have undisclosed problems.

**2/A.** The *in vitro* activity of cefiderocol against *Achromobacter xylosoxidans* 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  $\leq 0.5$  mg/L (zone diameter  $\geq 26$  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.

**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  $\leq 0.5$  mg/L (zone diameter  $\geq 28$  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.

<https://www.eucast.org/ast-of-bacteria/warnings>

The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 15.0, 2024. <http://www.eucast.org>.

# EUCAST Guidance Document on *S. maltophilia*

## – *Stenotrophomonas maltophilia*

### Conclusions and guidance

There is only weak evidence to support treatment alternatives in *S. maltophilia* infections. Historically trimethoprim-sulfamethoxazole has been regarded the drug of choice, but retrospective clinical data question whether this agent is preferable to other agents.

Alternatives which have been tried and discussed are fluoroquinolones (mainly levofloxacin and moxifloxacin), intravenous minocycline and cefiderocol, but there is scant or no clinical evidence for the usefulness of either of these or for a correlation between susceptibility test results and clinical outcome. Tigecycline may also be an option where intravenous minocycline is unavailable. The role of fluoroquinolones is challenging to assess due to unfavourable PK/PD despite meta-analyses and other studies suggesting superiority to trimethoprim-sulfamethoxazole.

Currently, cefiderocol is the agent with the most favourable *in vitro* activity and may be preferable to the traditional trimethoprim-sulfamethoxazole as first line therapy. However, uncertainty will persist until there are clinical studies to support this conclusion [40]. In summary, the efficacy of all agents and combinations is uncertain and treating physicians should be vigilant in case therapeutic responses are unconvincing.

## Guidance Document on *Stenotrophomonas maltophilia*

Version 2, November 2024

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journal homepage: [www.elsevier.com/locate/cmicom](http://www.elsevier.com/locate/cmicom)



Narrative Review

Rationale for contemporary antimicrobial treatment of *Stenotrophomonas maltophilia*: a narrative review

John Turnidge<sup>a</sup>, Sören Gatermann<sup>b,c</sup>, Gunnar Kahlmeter<sup>c,d</sup>, Rafael Cantón<sup>d</sup>, Mandy Wootton<sup>e</sup>, Christian G. Giske<sup>f,g</sup>, on behalf of the European Committee on Antimicrobial Susceptibility Testing



Guidance Document on *Stenotrophomonas maltophilia*, Version 2. [www.eucast.org](http://www.eucast.org)

The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 15.0, 2025. <http://www.eucast.org>. <https://doi.org/10.1016/j.cmicom.2025.105082>

# EUCAST Clinical Breakpoints v. 15.0

## – *Stenotrophomonas maltophilia*

- Cefiderocol siehe oben, Aztreonam/Avibactam IE
- Fluorochinolone (Ciprofloxacin, Levofloxacin)

Guidance Document on *Stenotrophomonas maltophilia*

Version 2, November 2024

### Notes

Numbered notes relate to general comments and/or MIC breakpoints.  
Lettered notes relate to the disk diffusion method.

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.



Check Zulassung Testsystem

„Levofloxacin: Kein Hinweis auf erworbene Resistenz. Die Substanz kann in Kombination als Therapieoption in Betracht gezogen werden.“



- Tetracycline:

Tetracyclines	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU		S ≥	R <	ATU	
Minocycline	Note <sup>1,2</sup>	Note <sup>1,2</sup>			Note <sup>A</sup>	Note <sup>A</sup>		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 <sup>1</sup>	Note <sup>1</sup>			Note <sup>A</sup>	Note <sup>A</sup>		

Guidance Document on *Stenotrophomonas maltophilia*, Version 2. [www.eucast.org](http://www.eucast.org)

The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 15.0, 2025.  
<http://www.eucast.org>.

# Validation von eingesetzten Testsystemen

## Spezies und Konzentrationsbereich

### 11. General warning against incomplete species validation and concentration range validation of commercially available susceptibility testing material and devices.

In many cases manufacturers of susceptibility testing material and devices list species for which the product is validated for use. This is in the package insert and by necessity often in fine print. The user of AST products and material is advised to insist on obtaining information and background data on the conditions (atmosphere, temperature etc) and for which species the product is intended for use. **In the absence of specific information on the procedure for and extent of validation, the product should NOT be used for the species.**

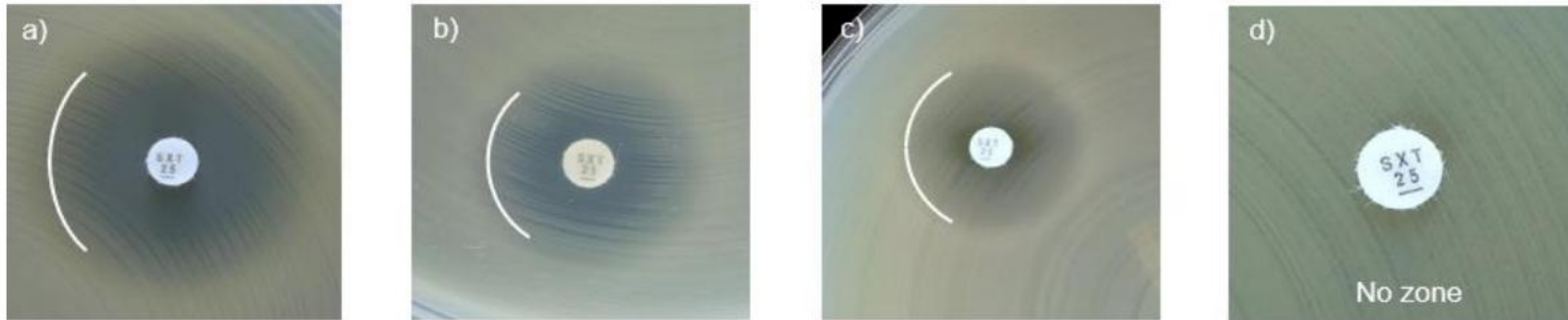
The user of products should also obtain information from the manufacturer on which range of MIC concentrations (and thus susceptibilities) the product was validated. This is not always clear. /June 2022, September 2023, November 2023.

# EUCAST Clinical Breakpoints v. 15.0

- *Stenotrophomonas maltophilia*
  - SXT: Neue BP (50/16 mm; 0,001/2 mg/L)

## Guidance Document on *Stenotrophomonas maltophilia*

Version 2, November 2024



**Examples of inhibition zones for *Stenotrophomonas maltophilia* with trimethoprim-sulfamethoxazole.**  
a-c) An outer zone can be seen. Read the outer zone edge and interpret according to the breakpoints.  
d) Growth up to the disk **and** no sign of inhibition zone. Report resistant.

Guidance Document on *Stenotrophomonas maltophilia*, Version 2. [www.eucast.org](http://www.eucast.org)

The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 15.0, 2025.  
<http://www.eucast.org>.

# EUCAST

## Clinical Breakpoints v. 15.0

- *Staphylococcus spp.*
  - Cephalosporine generell: Einarbeitung des neuen Guidance Dokuments

**1/A.** Susceptibility of staphylococci to cephalosporins is inferred from the cefoxitin susceptibility except for cefixime, ceftazidime, ceftazidime-avibactam, ceftibuten and ceftolozane-tazobactam, which do not have breakpoints and should not be used for staphylococcal infections. For agents given orally, care to achieve sufficient exposure at the site of the infection should be exercised. If cefotaxime and ceftriaxone are reported for methicillin-susceptible staphylococci, these should be reported "Susceptible, increased exposure" (I). Some methicillin-resistant *S. aureus* are susceptible to ceftaroline and ceftobiprole, **see Notes 7/D and 9/F.**

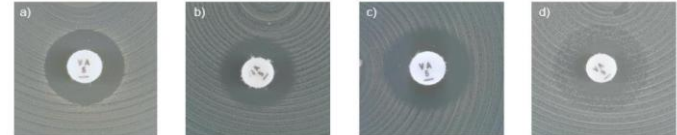
- Ceftarolin und Ceftobiprol: Ableitung S bei MSSA zulässig
- Dalbavancin: BP 0,25/0,25 mg/L; keine Ableitung von Vancomycin und Teicoplanin mehr möglich

# EUCAST Clinical Breakpoints v. 15.0

- *Enterococcus* spp.:
  - Neue Erläuterung zur Gültigkeit der BP bezogen auf Spezies

The *Enterococcus* genus includes several species besides those most commonly recovered from clinical samples, e.g. *E. faecalis* and *E. faecium*, namely *E. avium*, *E. casseliflavus*, *E. durans*, *E. gallinarum*, *E. hirae*, *E. lactis*, *E. mundtii* and *E. raffinosus*. Unless otherwise stated, breakpoints listed below are valid for all mentioned species.

- Dadurch:
  - Imipenem BP nur für *E. faecalis*
  - Vancomycin
    - Keine Vancomycin BP für *E. casseliflavus* und *gallinarum*
    - Unterschiedliche BP für *E. faecalis* und *E. faecium* bzw. sonstige Enterokokken
  - Neu BP für Tigecyclin (20/20 mm, 0,5/0,5 mg/L) und Eravacyclin (22/22 mm; 0,25/0,25 mg/L)



Examples of inhibition zones for *Enterococcus faecalis* and *E. faecium*, with vancomycin.

a) Sharp zone edge and zone diameter  $\geq 12$  mm. Report susceptible.

b-d) Fuzzy zone edge or colonies within zone. Perform confirmatory testing with PCR or report resistant even if the zone diameter  $\geq 12$  mm.

# EUCAST

## Clinical Breakpoints v. 15.0

- *Enterococcus* spp. neue BP für Aminopenicilline

Amoxicillin oral (uncomplicated UTI only)	4/4	standard dose 0.5 g x 3 oral
Amoxicillin oral <i>E. faecalis</i> only (other indications)	(0.001)/(4)	high dose: 0.75-1 g x 4 oral Oral amoxicillin has been used as follow-up therapy in some enterococcal infections, such as endocarditis or PJI. Particular attention must be paid to correct dosing in such indications.

- Keine BP für „systemic infections originating from the urinary tract“ da keine Daten verfügbar: Anwendung von (BP) für “other indications”
- Orale Anschluss Therapie: Anwendung von (BP) für “other indications”
- Orale Therapie nur BP für *E. faecalis*, da *E. faecalis* und *faecium* dominieren und letzterer in der Regel R ist

# EUCAST guidance document on Infective Endocarditis: Reporting of antimicrobial susceptibility testing results



## EUCAST guidance document on Infective Endocarditis:

### Reporting of antimicrobial susceptibility testing results

July 2025

- IE Behandlung benötigt höhere Dosen als Standard/High Dosen gemäß EUCAST
- Keine Kategorie I
- Basierend auf ECOFFs (außer Penicillin-Kombinationstherapie bei VSC)
- Basierend auf ESC Guidelines

# EUCAST guidance document on Infective Endocarditis: Reporting of antimicrobial susceptibility testing results

- In der ESC Guideline angeführte Substanzen für Viridans-Streptokokken, andere Streptokokken, *Staphylococcus* spp., *Enterococcus* spp., *Haemophilus influenzae* und *Kingella kingae* wurden berücksichtigt. Zusätzlich auch Substanzen für orale Follow-up Therapie.
- Generelle Empfehlung:
  - Sowohl Disc-Diffusion als auch MHK Methoden möglich (Mitteilung einer MHK ist nicht notwendig)
  - Ceftriaxon wird zwar in Kombination mit Aminopenicillinen bei Enterokokken-Endokarditis verwendet. Austestung wird aber nicht empfohlen (intrinsisch R)
- Orale Follow-up Therapie:
  - Bei Drug-Bug Kombinationen ohne BP (Moxifloxacin – EK, Rifampicin – VSC): ECOFF zum Ausschluss erworbener Resistenzmechanismen verwenden (kein S)
  - Keine Empfehlung für *Enterococcus* spp. und Rifampicin wegen hohem ECOFF und fehlender Evidenz

# Guidance document on use of daptomycin to treat enterococcal bloodstream infection and endocarditis

## Guidance document on use of daptomycin to treat enterococcal bloodstream infection and endocarditis

Updated April 2025

(minor revision to ensure concordance with endocarditis breakpoints and treatment guidelines)

### MIC distributions

MIC distributions for the wild-type populations of *Enterococcus faecalis* and *Enterococcus faecium* determined using EUCAST methods. ECOFFs are 4 mg/L and 8 mg/L, respectively (Table 2). Limited MIC distribution data exist for species other than *E. faecalis* and *E. faecium* at the time of publication (April 2025), but available data (Table 2) indicate that *Enterococcus* species in general exhibit wild-type MIC values of 0.5 – 4 mg/L.

Table 2: MIC distributions and epidemiological cut-off values (mg/L) for *Enterococcus* spp.

Species	Dist	≤0.06	0.125	0.25	0.5	1	2	4	8	≥16	ECOFF
<i>E. avium</i>	1				15	5					
<i>E. casseliflavus</i>	1				9	9	2				
<i>E. durans</i>	1		3	7	7	2	2	1			
<i>E. faecalis</i>	16	11	99	524	3794	10066	5148	525	16	10	4
<i>E. faecium</i>	16	5	39	66	198	988	11228	3308	230	7	8
<i>E. gallinarum</i>	1				3	10	6	1			
<i>E. hirae</i>	1				2	16	2				
<i>E. lactis</i>	1				2	14	4				
<i>E. mundtii</i>	1				2	5	2	2			
<i>E. raffinosus</i>	1			3	14	3					

Data from EUCAST MIC distribution website, April 2025

The balance of evidence from these studies suggests that better outcomes are usually achieved with high dose regimens of ≥9-10 mg/kg/day.

For enterococcal species other than *E. faecalis* and *E. faecium* there is not enough clinical and PK-PD data to allow guidance regarding daptomycin use [13, 14].

### Clinical outcome studies in endocarditis

Most enterococcal endocarditis is caused by *E. faecalis*. Published experience in treating endocarditis is more limited than that of bacteraemia. In a small series (n=6), Cerón et al. showed that daptomycin at 6-10 mg/kg/day was effective treatment [15]. Similar results were seen in another international study in *E. faecalis* endocarditis (n=9) with doses of 7.7-10.0 mg/kg/day [1616]. Kullar et al. reported good success with vancomycin-resistant *E. faecium* endocarditis (n=5) when daptomycin was given as doses of 8.2-10.0 mg/kg/day [17].

The European Society of Cardiology (ESC) guidelines [18] for management of endocarditis recommend combination therapy with a beta-lactam or fosfomycin, when daptomycin is used in enterococcal endocarditis treatment.

### Summary

High dose daptomycin has been thought to be effective in the treatment on enterococcal bloodstream infection and endocarditis, although published experience with the latter condition is limited. Although daptomycin is increasingly used for these conditions, especially when caused by vancomycin-resistant isolates, the EUCAST Steering Committee recognises that there are remaining uncertainties, particularly the inability of even the highest published doses (12 mg/kg/day) to achieve adequate exposure against all wild-type isolates of *E. faecalis* and *E. faecium*. The documented variation in susceptibility testing amplifies these uncertainties. Therefore, EUCAST has not proposed clinical breakpoints for daptomycin and *Enterococcus* species, but rather listed the breakpoint as "IE" = Insufficient Evidence. In part, this decision is influenced by the dosing regimen that is required for bloodstream far exceeds that of the regimen licensed by EMA.

EUCAST has detailed its position on the use of daptomycin in infections caused by *Enterococcus faecalis* and *E. faecium* in a publication in CMI (currently available at [https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(20\)30235-4/pdf](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30235-4/pdf)).

# EUCAST Clinical Breakpoints v. 15.0

- Beta-hämolysierende Streptokokken A, B, C, G
  - Neue BP für Benzylpenicillin abhängig von Serogruppe (ECOFFs unterschiedlich)

Penicillins <sup>1</sup>	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Benzylpenicillin <sup>2</sup> , Streptococcus groups A, C and G	0.03	0.03		1 unit	23	23	
Benzylpenicillin <sup>2</sup> , <i>S. agalactiae</i> (group B streptococci)	0.125	0.125		1 unit	18	18	
Ampicillin	Note <sup>1</sup>	Note <sup>1</sup>			Note <sup>A</sup>	Note <sup>A</sup>	
Ampicillin-sulbactam <sup>3</sup>	Note <sup>1</sup>	Note <sup>1</sup>			Note <sup>A</sup>	Note <sup>A</sup>	

## Notes

Numbered notes relate to general comments and/or MIC breakpoints.

Lettered notes relate to the disk diffusion method.

**1/A.** The susceptibility of streptococcus groups A, B, C and G to penicillins is inferred from the benzylpenicillin susceptibility (~~indications other than meningitis~~)-with the exception of phenoxymethylpenicillin and isoxazolylpenicillins for streptococcus group B, where there is insufficient evidence for clinical efficacy.

**2.** Resistant isolates are rare or not yet reported. The identification and antimicrobial susceptibility test result on any such isolate must be confirmed and the isolate sent to a reference laboratory.

**3.** The addition of a beta-lactamase inhibitor does not add clinical benefit.

- Neu BP Rifampicin (21/21 mm; 0,25/0,25 mg/L)

# EUCAST Clinical Breakpoints v. 15.0

## – Pneumokokken

- Einarbeitung Endokarditis Guidance Document (Penicilline, Cefotaxim, Ceftriaxon)
- Neuer Algorithmus zum Ausschluß von Beta-Laktam-Resistenzmechanismen

Penicillins <sup>1</sup>	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU		S ≥	R <	ATU	
<b>Benzyloxacillin</b> (indications other than endocarditis and meningitis)	0.06	1		1 unit <sup>A</sup>	Note <sup>A,B</sup>	Note <sup>A,B</sup>		<p>Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.</p> <p><b>1/B.</b> The oxacillin 1 µg disk diffusion screening test or a benzyloxacillin MIC test shall be used to exclude beta-lactam resistance mechanisms. When the screen is negative (oxacillin zone diameter ≥20 mm, or benzyloxacillin MIC ≤0.06 mg/L) all beta-lactam agents for which clinical breakpoints are available, including those with "Note" can be reported susceptible without further testing, except for cefaclor, which if reported, should be reported as "susceptible, increased exposure" (I). When the screen is positive (zone diameter &lt;20 mm, or benzyloxacillin MIC &gt;0.06 mg/L), <b>see flow chart below.</b></p> <p><b>2- For breakpoints and dosing in pneumonia, see table of dosages.</b></p> <p><b>2.</b> The addition of a beta-lactamase inhibitor does not add clinical benefit.</p> <p><b>3/C.</b> Susceptibility inferred from ampicillin (indications other than endocarditis and meningitis).</p> <p><b>4.</b> For susceptibility testing purposes, the concentration of clavulanic acid is fixed at 2 mg/L.</p> <p><b>A.</b> Read and interpret the benzyloxacillin disk only for isolates with oxacillin 1 µg zone diameters &lt;20 mm. If benzyloxacillin zone ≥14 mm, report benzyloxacillin "susceptible, increased exposure" (I). If zone &lt;14 mm, report benzyloxacillin resistant (R). <b>see flow chart below.</b></p> <p><b>D.</b> For interpretation of the oxacillin disk screen, see flow chart below.</p>
<b>Benzyloxacillin</b> (endocarditis and meningitis)	0.06	0.06			Note <sup>B</sup>	Note <sup>B</sup>		
<b>Ampicillin</b> (indications other than endocarditis and meningitis)	0.5	1		2	22	19		
<b>Ampicillin iv</b> (endocarditis and meningitis)	0.5	0.5			Note <sup>B</sup>	Note <sup>B</sup>		
<b>Ampicillin-sulbactam</b> <sup>2</sup>	Note <sup>1,3</sup>	Note <sup>1,3</sup>			Note <sup>B,C</sup>	Note <sup>B,C</sup>		
<b>Amoxicillin iv</b> (indications other than endocarditis and meningitis)	Note <sup>1,3</sup>	Note <sup>1,3</sup>			Note <sup>B,C</sup>	Note <sup>B,C</sup>		
<b>Amoxicillin iv</b> (endocarditis and meningitis)	0.5	0.5			Note <sup>B</sup>	Note <sup>B</sup>		
<b>Amoxicillin oral</b>	0.5	1			Note <sup>B,C</sup>	Note <sup>B,C</sup>		
<b>Amoxicillin-clavulanic acid iv</b> <sup>2</sup>	Note <sup>1,3</sup>	Note <sup>1,3</sup>			Note <sup>B,C</sup>	Note <sup>B,C</sup>		
<b>Amoxicillin-clavulanic acid oral</b> <sup>2</sup>	0.5 <sup>4</sup>	1 <sup>4</sup>			Note <sup>B,C</sup>	Note <sup>B,C</sup>		
<b>Piperacillin</b>	Note <sup>1,3</sup>	Note <sup>1,3</sup>			Note <sup>B,C</sup>	Note <sup>B,C</sup>		
<b>Piperacillin-tazobactam</b> <sup>2</sup>	Note <sup>1,3</sup>	Note <sup>1,3</sup>			Note <sup>B,C</sup>	Note <sup>B,C</sup>		
<b>Ticarcillin-clavulanic acid</b>	-	-			-	-		
<b>Temocillin</b>	-	-			-	-		
<b>Phenoxymethylpenicillin</b>	Note <sup>1</sup>	Note <sup>1</sup>			Note <sup>B</sup>	Note <sup>B</sup>		
<b>Oxacillin</b> (screen only) <sup>1</sup>	NA	NA		1	20 <sup>D</sup>	20 <sup>D</sup>		

# EUCAST Clinical Breakpoints v. 15.0

***Streptococcus pneumoniae***  
Expert Rules and Expected Phenotypes

Guidance documents

EUCAST Clinical Breakpoint Tables v. 15.0, valid from 2025-01-01  
For abbreviations and explanations of breakpoints, see the Notes sheet

## ***Streptococcus pneumoniae*: Flow chart based on screen tests for beta-lactam resistance mechanisms**

Following the flow chart avoids delays in reporting benzylpenicillin susceptibility in *S. pneumoniae*.  
Include both the oxacillin (1 µg) and the benzylpenicillin (1 unit) disks already from the beginning.  
Read and interpret the benzylpenicillin disk **only** for isolates with oxacillin zones <20 mm.

See the EUCAST warning on the use of benzylpenicillin gradient tests at <https://www.eucast.org/warnings/>.



S/I/R  
MHK nicht  
notwendig

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

**Oxacillin 1 µg zone diameter ≥20 mm  
(or benzylpenicillin MIC ≤0.06 mg/L)**

**Mechanism:** excludes all beta-lactam resistance mechanisms

**Report susceptible (S)** to beta-lactam agents for which clinical breakpoints are available, including those with "Note".  
**Exception:** Cefaclor is reported "susceptible, increased exposure" (I).

**No further testing required.**

**Oxacillin 1 µg zone diameter <20 mm  
(or benzylpenicillin MIC >0.06 mg/L)**

**Mechanism:** beta-lactam resistance detected

**Report resistant (R)** to benzylpenicillin in endocarditis and meningitis and to phenoxymethylpenicillin (all indications).

**For benzylpenicillin in indications other than endocarditis and meningitis,**  
read and interpret the benzylpenicillin disk;  
If zone ≥14 mm, report benzylpenicillin "susceptible, increased exposure" (I).  
If zone <14 mm, report benzylpenicillin resistant (R).

**For other beta-lactam agents, see below.**

**Oxacillin 1 µg zone diameter 9-19 mm**

Report susceptible (S) without further testing to: ampicillin, amoxicillin and piperacillin (without and with beta-lactamase inhibitor), cefepime, cefotaxime, ceftaroline, ceftobiprole, ceftriaxone, imipenem and meropenem.

For beta-lactam agents not listed, perform susceptibility test and interpret according to breakpoints.

**Oxacillin 1 µg zone diameter <9 mm**

For beta-lactam agents other than benzylpenicillin, perform susceptibility testing and interpret according to breakpoints.

**Warning against the use of gradient tests for benzylpenicillin MIC in *Streptococcus pneumoniae*.** Updated 20 August, 2025

EUCAST benzylpenicillin breakpoints in *Streptococcus pneumoniae* are ≤0.06 mg/L, R>1 mg/L for indications other than meningitis. Isolates which are positive in the screen for beta-lactam resistance (with the oxacillin 1 µg disk) have benzylpenicillin MIC values above 0.06 mg/L and are categorized either "susceptible, increased exposure", in which case isolates can be treated with benzylpenicillin if dosing is adjusted according to the MIC value, or resistant (R>1 mg/L), in which case benzylpenicillin, and often many other beta-lactam agents, should be avoided for treatment.

Until 2024, the EUCAST recommendation was to perform MIC determination for benzylpenicillin on all screen positive isolates. In 2024, EUCAST published zone diameter breakpoints for benzylpenicillin 1 unit to be used in screen positive isolates to categorise benzylpenicillin as "susceptible increased exposure" or "resistant". For laboratories still using MIC determination for benzylpenicillin SIR categorisation in *S. pneumoniae*, it is important to perform this with validated and accepted methods. This is especially important in isolates for which benzylpenicillin MICs are in the range 0.5 – 4 mg/L.

Following questions from NEQAS, EARS-Net and EUCAST users, the EDL investigated the accuracy of benzylpenicillin gradient tests TestM™ (bioMérieux) and MFS™ (Liofilchem). Both were tested on in-house prepared MH-F agar from Oxoid (Thermo Fisher Scientific) och BBL (BD). Broth microdilution using Mueller-Hinton-F (MH-F) broth was used as the reference.

**Both gradient tests were found to frequently underestimate MIC values by one or more doubling dilutions.** In the area around the R breakpoint (0.5 – 4 mg/L), and with some variation between the MH-F media and the two tests, 0 – 37% of values were on the reference MIC, 63 – 100 % were below and 0-10 % of the values above the reference MIC. Thus a clear negative bias in the test results. This is especially detrimental in the area close to the R breakpoint. Laboratories using gradient tests must be aware of this and MIC values of 0.5 - 4 mg/L should be checked with broth microdilution.

The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 15.0, 2025. <http://www.eucast.org>.

[https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST\\_files/Warnings/Warnings\\_docs/Warning\\_-\\_gradient\\_for\\_benzyl\\_and\\_pnc\\_August\\_2025\\_FINAL.pdf](https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Warnings/Warnings_docs/Warning_-_gradient_for_benzyl_and_pnc_August_2025_FINAL.pdf)



# Grundlage für den neuen Algorithmus

P1458

## Combining oxacillin and benzylpenicillin disk diffusion to categorise benzylpenicillin susceptibility in *Streptococcus pneumoniae* without MIC testing

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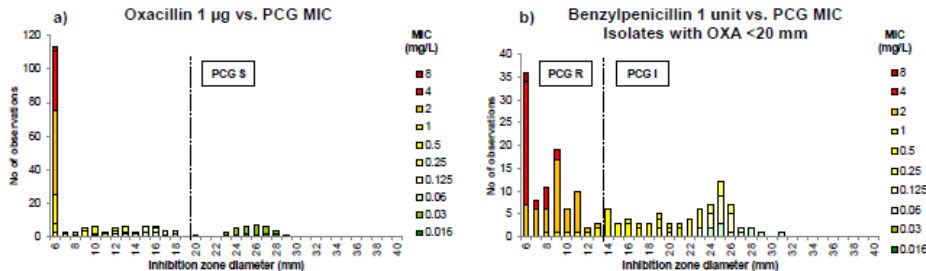


Figure 1. Inhibition zone diameter distribution with corresponding MIC values as coloured bars for *Streptococcus pneumoniae*.

a) The standard screening test for beta-lactam resistance with oxacillin 1 µg, which can be used to report benzylpenicillin as S (100 isolates).

b) The proposed follow-up test with benzylpenicillin 1 unit to distinguish between I and R for benzylpenicillin in *S. pneumoniae* with oxacillin 1 µg zones <20 mm (84 isolates).

Green = susceptible (S), yellow = “susceptible, increased exposure” (I), orange/red = resistant (R). The dotted lines shows the EUCAST zone diameter breakpoints.

# EUCAST Clinical Breakpoints v. 15.0

- Viridans Streptokokken
  - Einarbeitung Endokarditis Guidance Document (Penicilline)

Penicillins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU		S ≥	R <	ATU	
<b>Benzylpenicillin (screen only)</b>	0.25 <sup>1</sup>	0.25 <sup>1</sup>		1 unit	21 <sup>A</sup>	21 <sup>A</sup>		Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method. 1/A. Benzylpenicillin (MIC or disk diffusion) can be used to screen for beta-lactam resistance in viridans group streptococci. Isolates categorised as screen negative can be reported susceptible to beta-lactam agents for which clinical breakpoints are listed (including those with "Note"). Isolates categorised as screen positive should be tested for susceptibility to individual agents or reported resistant. 2/B. For information on how to use breakpoints in brackets, see <a href="https://www.eucast.org/eucastguidancedocuments/">https://www.eucast.org/eucastguidancedocuments/</a> . 3. The addition of a beta-lactamase inhibitor does not add clinical benefit. 4/C. For benzylpenicillin screen negative isolates, susceptibility can be inferred from benzylpenicillin or ampicillin. For benzylpenicillin screen positive isolates, susceptibility is inferred from ampicillin. D. Susceptibility can be inferred from the benzylpenicillin screen test or from "Ampicillin iv (endocarditis)".
<b>Benzylpenicillin (indications other than endocarditis)</b>	0.25	1		1 unit	21	12		
<b>Benzylpenicillin (endocarditis)</b>	0.25	0.25			21	21		
<b>Benzylpenicillin (endocarditis, in combination with other antimicrobial treatment)</b>	(1) <sup>2</sup>	(1) <sup>2</sup>			(12) <sup>B</sup>	(12) <sup>B</sup>		
<b>Ampicillin (indications other than endocarditis)</b>	0.5	2		2	21	15		
<b>Ampicillin iv (endocarditis)</b>	0.5	0.5		2	21	21		
<b>Ampicillin-sulbactam<sup>3</sup></b>	Note <sup>1,4</sup>	Note <sup>1,4</sup>			Note <sup>A,C</sup>	Note <sup>A,C</sup>		
<b>Amoxicillin (indications other than endocarditis)</b>	0.5	2			Note <sup>A,C</sup>	Note <sup>A,C</sup>		
<b>Amoxicillin iv (endocarditis)</b>	0.5	0.5			Note <sup>A,D</sup>	Note <sup>A,D</sup>		
<b>Amoxicillin-clavulanic acid<sup>3</sup></b>	Note <sup>1,4</sup>	Note <sup>1,4</sup>			Note <sup>A,C</sup>	Note <sup>A,C</sup>		
<b>Piperacillin</b>	Note <sup>1,4</sup>	Note <sup>1,4</sup>			Note <sup>A,C</sup>	Note <sup>A,C</sup>		
<b>Piperacillin-tazobactam<sup>3</sup></b>	Note <sup>1,4</sup>	Note <sup>1,4</sup>			Note <sup>A,C</sup>	Note <sup>A,C</sup>		

Basierend auf ECOFFS (außer Kombinationstherapie)  
Kein I

- Linezolid: keine Breakpoints, aber Hinweis zum Ausschluss erworbener Resistenz

**1. Linezolid has been used in oral follow-up treatment of endocarditis caused by viridans group streptococci. There are no clinical breakpoints but acquired resistance (isolates with MIC >2 mg/L) should be excluded. When excluded, the isolate should be reported "devoid of linezolid resistance mechanisms", but not as susceptible to linezolid.**

# EUCAST guidance document on Infective Endocarditis: Reporting of antimicrobial susceptibility testing results

## – Benzylpenicillin 1U als Screening für Beta-Laktam Resistenz

Benzylpenicillin 1U disk can be used to screen for  $\beta$ -lactam resistance. Screen-negative isolates can be reported susceptible to the following relevant  $\beta$ -lactams: benzylpenicillin, ampicillin, amoxicillin, cefotaxime, ceftriaxone, and carbapenems). For screen-positive isolates, the agent intended for treatment should be subjected to antimicrobial susceptibility testing.

## – Unklare Datenlage bei Endokarditisbehandlung mit Penicillin mit MHK 0,5-1 mg/L

EUCAST acknowledges that the evidence for treatment with benzylpenicillin of viridans group streptococci with benzylpenicillin MIC 0.5 - 1 mg/L is not clear. Therefore, these isolates should not be reported as susceptible, but rather with a comment that benzylpenicillin, when used for such isolates, should be combined with other active therapy. In the breakpoint table, this is displayed as an extra line for “Benzylpenicillin (endocarditis, in combination with other antimicrobial treatment)” with bracketed breakpoints. **Isolates with a benzylpenicillin disk diffusion test inhibition zone <12 mm, corresponding to an MIC>1 mg/L, should be reported as resistant to benzylpenicillin.**

# EUCAST Clinical Breakpoints v. 15.0

- Haemophilus influenzae
  - Einarbeitung Endokarditis Guidance Document (Penicilline)

Penicillins <sup>1</sup>	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU		S ≥	R <	ATU	
Benzylpenicillin	IE	IE			IE	IE		Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.  1/A. The benzylpenicillin 1 unit disk diffusion screening test shall be used to exclude beta-lactam resistance mechanisms. When the screen is negative (zone diameter ≥12 mm) all penicillins for which clinical breakpoints are available, including those with "Note", can be reported susceptible without further testing, except for amoxicillin oral and amoxicillin-clavulanic acid oral, which if reported, should be reported "susceptible, increased exposure" (I). When the screen is positive (zone diameter <12 mm), <b>see flow chart below</b> . 2. Beta-lactamase positive isolates can be reported resistant to ampicillin, amoxicillin and piperacillin without inhibitors. Tests based on a chromogenic cephalosporin can be used to detect the beta-lactamase. 3. For susceptibility testing purposes, the concentration of sulbactam is fixed at 4 mg/L. 4/D. Susceptibility can be inferred from amoxicillin-clavulanic acid iv. 5. For susceptibility testing purposes, the concentration of clavulanic acid is fixed at 2 mg/L. 6. For susceptibility testing purposes, the concentration of tazobactam is fixed at 4 mg/L.  B. Read the outer edge of zones where an otherwise clear inhibition zone contains an area of growth around the disk, <b>see pictures below</b> . C. ATU relevant only if the benzylpenicillin 1 unit disk screen is positive (zone diameter <12 mm). E. Susceptibility can be inferred from ampicillin. F. Isolates susceptible to ampicillin can be reported "susceptible, increased exposure" (I) to amoxicillin oral. Isolates resistant to ampicillin can be reported resistant to amoxicillin oral.
Benzylpenicillin (screen only) <sup>1</sup>	NA	NA		1 unit	12 <sup>A,B</sup>	12 <sup>A,B</sup>		
Ampicillin (indications other than endocarditis and meningitis) <sup>2</sup>	1	1		2	18 <sup>A,B</sup>	18 <sup>A,B</sup>		
Ampicillin iv (endocarditis and meningitis) <sup>2</sup>	IE	IE			IE	IE		
Ampicillin-sulbactam	1 <sup>3,4</sup>	1 <sup>3,4</sup>			Note <sup>A,D</sup>	Note <sup>A,D</sup>		
Amoxicillin iv (indications other than endocarditis and meningitis) <sup>2</sup>	2	2			Note <sup>A,E</sup>	Note <sup>A,E</sup>		
Amoxicillin iv (endocarditis and meningitis) <sup>2</sup>	IE	IE			IE	IE		
Amoxicillin oral <sup>2</sup>	0.001	2			Note <sup>A,F</sup>	Note <sup>A,F</sup>		
Amoxicillin-clavulanic acid iv	2 <sup>5</sup>	2 <sup>5</sup>		2-1	15 <sup>A,B</sup>	15 <sup>A,B</sup>		
Amoxicillin-clavulanic acid oral	0.001 <sup>5</sup>	2 <sup>5</sup>		2-1	50 <sup>A,B</sup>	15 <sup>A,B</sup>		
Piperacillin <sup>2</sup>	IE	IE			IE	IE		
Piperacillin-tazobactam	0.25 <sup>5</sup>	0.25 <sup>5</sup>		30-6	27 <sup>A,B</sup>	27 <sup>A,B</sup>	26-28 <sup>B,C</sup>	
Ticarcillin-clavulanic acid	IE	IE			IE	IE		
Temocillin	IE	IE			IE	IE		

- Cefepim-Enmetazobactam: keine BP, da Ableitung von Cefepim
- Ciprofloxacin: Neuer BP (32/32 mm; 0,03/0,03 mg/L)

# EUCAST Clinical Breakpoints v. 15.0

- *Moraxella catarrhalis*
  - Cefepim-Enmetazobactam: keine BP, da Ableitung von Cefepim
- *Bacteroides spp.*
  - Hinweis Piperacillin-Tazobactam
    - 3. Isolates susceptible to ampicillin-sulbactam and amoxicillin-clavulanic acid may be resistant to piperacillin-tazobactam.**
- *Fusobacterium necrophorum*
  - Benzylpenicillin: neue MHK BP 0,125/0,125 mg/L
- *Kingella kingae*

Amoxicillin-clavulanic acid	Note <sup>3</sup>	Note <sup>3</sup>		2-1	22	22		<small>           4A. Susceptibility can be inferred from benzylpenicillin susceptibility.            3. The <i>in vitro</i> antimicrobial activity of the fixed concentration of 2 mg/L for clavulanic acid is such that artefactually low MIC values may be obtained. Therefore no breakpoints can be given. This does not affect disk diffusion where the concentration of the inhibitor decreases proportionally with the concentration of the agent.         </small>
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# EUCAST Clinical Breakpoints v. 15.0

## PK/PD cut-off values

## EUCAST Clinical Breakpoint Tables v. 15.0, valid from 2025-01-01

Pharmacokinetics and pharmacodynamics (PK/PD) are important, but not the only tools for setting and revising clinical breakpoints. PK/PD targets are often based on a limited number of species. The selection of clinical PK/PD targets is highly dependent on the targeted patient population. Critically ill patients or immunocompromised patients will normally require higher antimicrobial exposure, and thus the PK/PD targets will be higher. As clinical PK/PD targets are often lacking, preclinical PK/PD targets determined in *in vitro* and animal models are often used. These models are not always validated with clinical data. Moreover, the animal models are usually limited to the neutropenic mouse thigh and lung infection model and may not have a translational value for all type of infections. Different PK/PD targets can be determined depending on i) the species, ii) the level of effect (stasis, 1-3 log kill, prevention of emergence of resistance), and iii) the within-species strain variation of PK/PD-targets.

Moreover, simulated pharmacokinetics (healthy vs. patients, different patient populations with different degree of renal/hepatic insufficiencies, levels of plasma proteins and other important covariates) will play a major role in determining PK/PD cut-offs. Critically ill patients have much higher variation in PK than other groups of patients. Calculations are usually made based on free drug concentrations in the plasma or epithelial lining fluid, which are presumed to relate to the concentration at the site of infection. Individual variations in protein binding may also affect the pharmacodynamically important drug exposure. Finally, PK/PD cut-offs may be based on various levels of probability of target attainment like 99%, 95% or 90%. All these factors may result in different PK/PD cut-off values that span in several two-fold dilutions.

A common misunderstanding is that PK/PD cut-offs can be used when clinical breakpoints are lacking. This is not the intention. Instead EUCAST has developed guidance on “When there are no breakpoints” ([see EUCAST guidance document](#)) and removed the PK/PD cut-offs from the breakpoint tables. This is to underline that these values should never be used when clinical breakpoints are lacking.

European Committee on Antimicrobial Susceptibility Testing  
**Zone diameter breakpoint table for rapid antimicrobial susceptibility testing (RAST)  
 directly from blood culture bottles**

Version 8.1, valid from 2025-07-14

This document should be cited as "The European Committee on Antimicrobial Susceptibility Testing. Zone diameter breakpoint tables for rapid antimicrobial susceptibility testing (RAST) directly from blood culture bottles. Version 8.1, 2025. <http://www.eucast.org>."

<b>Version 8.1, 2025-07-14</b>	<b>Changes from v. 8.0 are marked light blue. Removed comments are shown in strikethrough font style.</b>
<i>S. pneumoniae</i>	<b>Revised breakpoints</b> • Typo corrected for benzylpenicillin
<b>Version 8.0, 2025-03-18</b>	<b>Changes from v. 7.2 are marked yellow. Changed comments are underlined. Removed comments are shown in strikethrough font style.</b>
<i>S. enterica</i>	<b>Revised comments</b> • Comment 1, specific screening cut-off for ESBL-producing <i>S. enterica</i> available • Comment 2, screening cut-off for carbapenemase production in <i>S. enterica</i> not available with the RAST method
<i>E. faecalis</i>	<b>Revised comments</b> • Information regarding intravenous treatment added to comment 1 • Piperacillin-tazobactam removed from comment 1
<i>E. faecium</i>	<b>Removed breakpoints</b> • Imipenem <b>Revised comments</b> • Information regarding intravenous treatment added to comment 1 • Piperacillin-tazobactam removed from comment 1
<i>S. pneumoniae</i>	<b>New breakpoints</b> • Benzylpenicillin in indications other than meningitis and endocarditis (separate table) <b>Revised comments</b> • Comment 2

**2. For oxacillin screen positive isolates, report benzylpenicillin resistant in meningitis and endocarditis. For other indications, see the table below.** If the oxacillin zone diameter is  $\geq 9$  mm (irrespective of incubation time 4, 6, 8 and 16-20 hours), report ampicillin, amoxicillin and piperacillin (with and without  $\beta$ -lactamase inhibitor), cefotaxime, ceftazidime, ceftaroline, ceftibiprole, cefepime, imipenem and meropenem, susceptible. For any other agent and when the oxacillin zone is  $< 9$  mm, perform an MIC for the agent considered for clinical use.

**In oxacillin screen positive isolates and for indications other than meningitis and endocarditis, read the benzylpenicillin 1 unit disk and interpret according to the table below.**

Antimicrobial agent	Disk content	4 hours			6 hours			8 hours			16-20 hours		
		S $\geq$	ATU	R $<$	S $\geq$	ATU	R $<$	S $\geq$	ATU	R $<$	S $\geq$	ATU	R $<$
<b>Benzylpenicillin (indications other than meningitis and endocarditis)</b>	<b>1 unit</b>	50	11-13	11	50	12-13	12	50	12-14	12	50	13-15	13

# EUCAST RAST

## Screening for ESBL and carbapenemases in *Escherichia coli*, *Klebsiella pneumoniae* and *Salmonella enterica* for epidemiological purposes as part of the RAST procedure.

EUCAST Guidelines for detection of resistance mechanisms and specific resistance of clinical and/or epidemiological importance using EUCAST rapid antimicrobial susceptibility testing (RAST) directly from positive blood culture bottles.

**Version 3.0**  
**March 2025**

### 2. Extended-spectrum $\beta$ -lactamase (ESBL)-producing *E. coli*, *K. pneumoniae* and *S. enterica*.

- With the RAST method, ESBL production in *E. coli*, *K. pneumoniae* and *S. enterica* can be detected by using cefotaxime and ceftazidime screening cut-off values at 4, 6, 8 and 16-20 hours.
- Test both cefotaxime and ceftazidime.
- Screen-positive organisms (for cefotaxime and/or ceftazidime) should be subjected to ordinary confirmatory and typing procedures.

Table 1. Screening cut-off values (mm) for ESBL-producing *E. coli*, *K. pneumoniae* and *S. enterica*.

Species	Antimicrobial agent	Conduct ESBL testing if			
		4 hours	6 hours	8 hours	16-20 hours
<i>E. coli</i>	Cefotaxime 5 $\mu$ g	<15	<16	<17	<16
	Ceftazidime 10 $\mu$ g	<15	<16	<17	<17
<i>K. pneumoniae</i>	Cefotaxime 5 $\mu$ g	<15	<18	<18	<16
	Ceftazidime 10 $\mu$ g	<15	<16	<16	<18
<i>S. enterica</i>	Cefotaxime 5 $\mu$ g	<13	<14	<14	<14
	Ceftazidime 10 $\mu$ g	<12	<16	<17	<18

# Qualitätskontrolle - How to make use of EUCAST MIC and zone distributions

- Verteilungen von MHK- und Zonendurchmesser sind bei EUCAST verfügbar
- Wenn genügend akzeptable Verteilungen zur Verfügung stehen, werden ECOFFs bestimmt und zusammen mit den Konfidenzintervallen unter jedem Diagramm aufgelistet
- Bei 50 – 100 phänotypischen Tests (MHK-Bestimmungen oder Diskdiffusion), kann eine eigene Verteilung erstellt werden. Diese kann mit der EUCAST-Referenzverteilung verglichen werden.
- Sofern der Wildtyp-Teil der Verteilung nicht mit dem EUCAST-Gegenstück deckungsgleich ist, muss die Methodik im jeweiligen Labor überprüft werden, bevor EUCAST-Grenzwerte verwendet werden.
- Diese Methode funktioniert nicht bei allen Erregern mit erworbenen Resistenzmechanismen

22.07.2025

## How to make use of EUCAST MIC and zone distributions

EUCAST distributions of MIC and Zone diameters (<https://mic.eucast.org>; choose either "MIC" or "Disk diffusion") are freely available. When sufficiently many acceptable distributions are available to the curators, ECOFFs are determined and listed beneath each graph together with confidence intervals. When users have performed 50 – 100 phenotypic tests (MIC determinations or disk diffusion), create your own distribution and check this against the EUCAST reference distribution. Unless the wild type part of the distribution is superimposable on the EUCAST counterpart, the methodology in the individual laboratory needs reconsideration before EUCAST breakpoints are used. A method which performs well with isolates in the wild type may on occasion perform less well on isolates with resistance mechanisms (bias). Every method needs to be challenged using strains with resistance mechanisms. Some examples of this are listed on the EUCAST [Warnings page](#). Trouble shoot and discuss with your [National AST Committee](#), or contact EUCAST. This text was amended and links added on 2 August, 2025.

# Ausblick 2026

- Neue Carbapenem BP für EB
  - Vorschlag für Befundkommentar

“If a carbapenemase is detected the clinical response to treatment with carbapenems may be impaired even in the absence of clinical resistance. Other novel antimicrobials should be preferred treatment, but if unavailable carbapenems could be considered if high exposure is used and/or in combination with a second active agent. Consider switching therapy in complicated infections.”

- Neue Fluorochinolon BP bei EB
  - Screening auf mittels Pefloxacin
- Verfügbarkeit von MH-F und FAA-Agar

## Proposed addition of a comment for carbapenemase-producing Enterobacterales

July 2025

11.09.2025

### Manufacturers of MH-F and FAA plates to contact EUCAST

Manufacturers and distributors of pre-poured MH-F and FAA agar plates for EUCAST susceptibility testing by disk diffusion of fastidious (medium MH-F with horse blood) and anaerobic species (medium FAA with horseblood) are encouraged to contact EUCAST. We have been asked to map the capability and capacity of manufacturers and distributors of these plates. The aim is for EUCAST to publish on its website a table or map informing laboratories as to the national/regional availability of media in different parts of the world.

EUCAST will start by compiling a list of relevant media manufacturers and distributors each of which will then be asked to respond to a short series of relevant questions. Report company name and contact information to EUCAST via [gunnar.kahlmeter\[at\]eucast.org](mailto:gunnar.kahlmeter[at]eucast.org).

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**Vielen Dank für die Aufmerksamkeit**