Ordens klinikum Linz
Barmherzige Schwestern Elisabethinen

EUCAST Update 2023

Nationales Referenzzentrum für antimikrobielle Resistenz (NRZ),
Institut für Hygiene, Mikrobiologie und Tropenmedizin
Ordensklinikum Linz Elisabethinen
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EIN UNTERNEHMEN DER VINZENZ GRUPPE
UND DER ELISABETHINEN

Inhalt

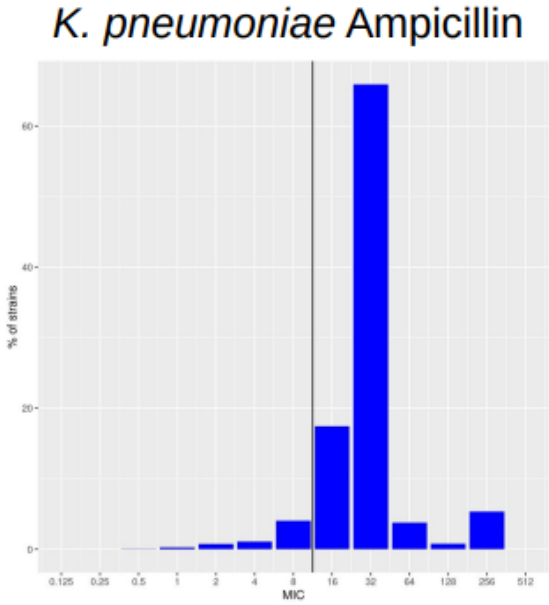
- expected phenotypes
- (-)
- Aminopenicilline und *Enterobacterales*
- Ciprofloxacin bei Meningitis
- Erythromycin und Tetracyclin Screen
- *Enterococcus spp.* BP
- Entfernung einiger „I“ Kategorien
- *Pasteurella spp.*
- *Corynebacterium diphteriae* und *ulcerans*
- Anaerobier
- What to do when there are no Breakpoints?
- RAST
- Status quo Fosfomycin
- Status quo Cefiderocol

Expected phenotypes

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- Was bedeutet „intrinsische Resistenz“?
  - „immer“ resistent? „normalerweise“ resistent?
- ersetzt durch **„expected phenotype“**
  - **expected resistant phenotype**:
    ≥ 90% „resistent“ getestet
  - **expected susceptible phenotype**:
    ≥ 99% „sensibel“ getestet

- Testung nicht notwendig
- unerwarteter Phänotyp: ID? Empfindlichkeitstestung? → ggf. weitere Abklärung



(“-“)

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Dash (“-“) in breakpoint tables indicates that the agent is unsuitable for treatment of systemic infections caused by the organism or group. For this reason EUCAST refrained from determining breakpoints and recommend that the agent is not included in susceptibility test reports. If included, report resistant without prior testing.

Enterobacterales: Aminopenicilline

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Clinical breakpoints - bacteria (v 12.0) – (**1 Jan - 31 Dec, 2022**)

Penicillins[1]	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.
Benzylpenicillin	-	-			-	-		1. Aminopenicillin breakpoints in *Enterobacterales* are based on intravenous administration. For oral administration the breakpoints are relevant for urinary tract infections only. Breakpoints for other infections are under review.
Ampicillin[1]	8	8		10	14[A]	14[A]		2. For susceptibility testing purposes, the concentration of sulbactam is fixed at 4 mg/L.
Ampicillin-sulbactam[1]	8[2]	8[2]		10-10	14[A]	14[A]		3. For susceptibility testing purposes, the concentration of clavulanic acid is fixed at 2 mg/L.
Amoxicillin[1]	8	8		-	Note[B]	Note[B]		4. For susceptibility testing purposes, the concentration of tazobactam is fixed at 4 mg/L.
Amoxicillin-clavulanic acid[1]	8[3]	8[3]		20-10	19[A]	19[A]	19-20	5. Agar dilution is the reference method for mecillinam MIC determination.
Amoxicillin-clavulanic acid (uncomplicated UTI only)	32[3]	32[3]		20-10	16[A]	16[A]		A. Ignore growth that may appear as a thin inner zone on some batches of Mueller-Hinton agars.
Piperacillin	8	8		30	20	20		B. Susceptibility inferred from ampicillin.
Piperacillin-tazobactam	8[4]	8[4]	16	30-6	20	20	19	C. Ignore isolated colonies within the inhibition zone.

- bisher nur für i.v. Aminopenicilline BP
- Ausnahme: orales Amoxicillin/Clavulansäure, BP ausschließlich für unkomplizierten Harnwegsinfekt (uUTI)

Clinical breakpoints v. 13.1 (2023)

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Enterobacterales*

EUCAST Clinical Breakpoint Tables v. 13.1, valid from 2023-06-29

Expert Rules and Expected Phenotypes

For abbreviations and explanations of breakpoints, see the Notes sheet

Penicillins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Benzylpenicillin	-	-			-	-	
Ampicillin iv[1]	8	8		10	14[A]	14[A]	
Ampicillin oral (uncomplicated UTI only)[1]	8	8		10	14[A]	14[A]	
Ampicillin-sulbactam iv[1]	8[2]	8[2]		10-10	14[A]	14[A]	
Ampicillin-sulbactam oral (uncomplicated UTI only)[1]	8[2]	8[2]		10-10	14[A]	14[A]	
Amoxicillin iv[1]	8	8		-	Note[B]	Note[B]	
Amoxicillin oral (infections originating from the urinary tract)[1]	0.001	8		-	Note[C]	Note[C]	
Amoxicillin oral (uncomplicated UTI only)[1]	8	8		-	Note[B]	Note[B]	
Amoxicillin oral (other indications)[1]	(8)[3]	(8)[3]		-	Note[B,E]	Note[B,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]	(8)[3,4]	(8)[3,4]		20-10	(19)[A,D]	(19)[A,D]	19-20
Piperacillin	8	8		30	20	20	
Piperacillin-tazobactam	8[5]	8[5]	16	30-6	20	20	19
~~Ticarcillin~~							
Ticarcillin-clavulanic acid	8[4]	16[4]		75-10	23	20	
Temocillin (infections originating from the urinary tract), *E. coli*, *Klebsiella* spp. (except *K. aerogenes*) and *P. mirabilis*	0.001	16		30	50[F]	17[F]	
Phenoxymethylpenicillin	-	-			-	-	

(infections originating from the urinary tract)". Isolates resistant to ampicillin (iv or oral) can be reported resistant to

12 Bewertungen für 4 Substanzen
Ampicillin
Amoxicillin
Ampicillin/ Sulbactam
Amoxicillin/ Clavulansäure

Formulierung
- oral, i.v.

Infektionsort: orale AP
- unkomplizierter Harnwegsinfekt
- Infektion ausgehend vom Harntrakt
- andere Indikationen

Hintergrund: Aminopenicilline und *Enterobacterales*

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Sind orale Aminopenicilline (AP) geeignet in der Therapie von Infektionen durch *Enterobacterales*?

– unterschiedlich schwer verlaufende Infektionen durch *Enterobacterales*
– erreichbare Exposition durch orale AP sehr viel geringer als i.v. AP

→ insbesondere bei systemischen Infektionen keine ausreichende Exposition durch orale AP

Hintergrund: Aminopenicilline und Enterobacterales

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Unterschiede p.o. und i.v.

- geringere orale Bioverfügbarkeit von Ampicillin im Vergleich zu Amoxicillin p.o.
- bei oraler Aufnahme von Amoxicillin von Dosen >750mg zunehmend geringer Resorption
- maximal erreichbare Exposition mit oralem Amoxicillin/Clavulansäure kann nur Pathogene mit einer MHK bis zu 2mg/l abdecken (Dosierung 3 x 875 mg Amoxicillin + 125mg Clavulansäure), der ECOFF der meisten *Enterobacerales* liegt allerdings bei 8mg/l

Hintergrund: Aminopenicilline und *Enterobacterales*

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- Konzentrierung von AP im Harn → Therapie uUTI
- orales Amoxicillin/Clavulansäure wichtig in der orale Sequenztherapie von Patienten mit Infektionen aus dem Harntrakt (z.B. Bakteriämie bei Pyelonephritis)
- Maximaldosis von oralem Amoxicillin/Clavulansäure inadäquat für andere systemische Infektionen durch *Enterobacterales* → wenig klinische Evidenz für Monotherapie

Implementierung der neuen Breakpoints

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

Guidance on the Implementation of Revised Aminopenicillin Breakpoints for *Enterobacterales*
January 2023

„…*reporting should be performed but this may have to be modified in accordance with national guidelines and traditions and/or the limitations imposed by local health care and laboratory information systems*.“

Enterobacterales und Aminopenicilline

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Penicillins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Benzylpenicillin	-	-			-	-	
Ampicillin iv[1]	8	8		10	14[A]	14[A]	
Ampicillin oral (uncomplicated UTI only)[1]	8	8		10	14[A]	14[A]	
Ampicillin-sulbactam iv[1]	8[2]	8[2]		10-10	14[A]	14[A]	
Ampicillin-sulbactam oral (uncomplicated UTI only)[1]	8[2]	8[2]		10-10	14[A]	14[A]	
Amoxicillin iv[1]	8	8		-	Note[B]	Note[B]	
Amoxicillin oral (infections originating from the urinary tract)[1]	0.001	8		-	Note[C]	Note[C]	
Amoxicillin oral (uncomplicated UTI only)[1]	8	8		-	Note[B]	Note[B]	
Amoxicillin oral (other indications)[1]	(8)[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]	(8)[3,4]	(8)[3,4]		20-10	(19)[A,D]	(19)[A,D]	19-20

uUTI → **S**
→ **andere BP** für Amoxi/Clav oral

originated from urinary tract → **„I“** für Amoxi, Amoxi/Clav oral

other indications ( )
→ **Kommentar**

i.v. Aminopenicilline unabhängig von der Indikation → S

Material: Harn

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Kultur :
nachgewiesene Keime :
1. Escherichia coli (10^7 KbE/ml)
Die Interpretation "Sensibel" bei Zusatz "oral" gilt nur für unkomplizierte Harnwegsinfektionen.
Aminoglykoside: Interpretation gültig für Harnwege. Bei systemischen Infektionen nur in Kombination verwenden.

Antibiogramm	1
Ampicillin oral	S
Amoxicillin-Clavulansäure oral	S
Amoxicillin-Clavulansäure iv	S
Mecillinam oral	S
Cefalexin oral	S
Cefuroxim oral	S
Cefotaxim	S
Ceftazidim	S
Cefepim	S
Meropenem	S
Ciprofloxacin	S
Gentamicin	S
Nitrofurantoin oral	S
Trimethoprim + Sulfonamid	S

Interpretation „Sensibel“ bei Zusatz „oral“ gilt nur für unkomplizierte Harnwegsinfektionen.

Material: Harn

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Kultur :
nachgewiesene Keime :
1. Escherichia coli (10^7 KbE/ml)
Die Interpretation "Sensibel" bei Zusatz "oral" gilt nur für unkomplizierte Harnwegsinfektionen.
Aminoglykoside: Interpretation gültig für Harnwege. Bei systemischen Infektionen nur in Kombination verwenden.

Antibiogramm	1
Ampicillin oral	R
Amoxicillin-Clavulansäure oral	S
Amoxicillin-Clavulansäure iv	R
Mecillinam oral	S
Cefalexin oral	S
Cefuroxim oral	S
Cefotaxim	S
Ceftazidim	S
Cefepim	S
Meropenem	S
Ciprofloxacin	S
Gentamicin	S
Nitrofurantoin oral	S
Trimethoprim + Sulfonamid	R

Beispiel: Blutkultur

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Kultur :
nachgewiesene Keime :
1. Escherichia coli
* Amoxicillin-Clavulansäure oral: Kein Hinweis auf erworbene Resistenz. Ausreichende Konzentration am Infektionsort sicherstellen und insbesondere bei systemischen Infektionen in Kombination verwenden.
Aminoglykoside: Interpretation gültig für Harnwege. Bei systemischen Infektionen nur in Kombination verwenden.

Antibiogramm	1
Ampicillin iv	S
Amoxicillin-Clavulansäure oral	*
Amoxicillin-Clavulansäure iv	S
Piperacillin-Tazobactam	S
Cefuroxim iv	I
Cefotaxim	S
Ceftazidim	S
Cefepim	S
Meropenem	S
Ciprofloxacin	S
Gentamicin	S
Trimethoprim + Sulfonamid	S

„orginated from urinary tract“
oder
„other indications“?

Beispiel: Wundabstrich

Kultur :
nachgewiesene Keime :
1. **Proteus mirabilis**(++)
* Amoxicillin-Clavulansäure oral: Kein Hinweis auf erworbene Resistenz. Ausreichende Konzentration am Infektionsort sicherstellen und insbesondere bei systemischen Infektionen in Kombination verwenden.
2. **Staphylococcus hominis**(nach Anreicherung)

Antibiogramm	1
Ampicillin iv	S
Amoxicillin-Clavulansäure oral	*
Amoxicillin-Clavulansäure iv	S
Cefuroxim iv	I
Cefotaxim	S
Ceftazidim	S
Cefepim	S
Meropenem	S
Ciprofloxacin	S
Trimethoprim + Sulfonamid	S

„other indications“ orale AP

Meningitis BP für Ciprofloxacin

Enterobacterales NEU

– bei Meningitis MHK-Testung von Ciprofloxacin (R > 0,125mg/L) oder Testung von Perfloxacin 5µg (Screen) (R < 24mm)

Haemophilus influenzae NEU

– bei Meningitis MHK-Testung von Ciprofloxacin (R > 0,03mg/l) oder Testung von Nalidixin 30µg (Screen) (R < 23mm)

Neisseria meningitidis

	(mg/L)		
	S ≤	R >	ATU
Ciprofloxacin (all indications, including meningitis and prophylaxis)	0.016	0.016	
Delafloxacin	IE	IE	

Makrolid und Tetrazyclin Screening

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- **Erythromycin** BP zusätzlich als Screening für Azithromycin, Clarithromycin, Roxithromycin bei *Staphylococcus spp*., *Streptococcus* group A,B,C,G, *Streptococcus pneumoniae, Moraxella catarrhalis*

- **Tetracyclin** BP zusätzlich als Screening für Doxycyclin (z.T. Minocyclin) *Staphylococcus spp., Streptococcus* group A,B,C,G, *Streptococcus pneumoniae*

Enterococcus spp.

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The *Enterococcus* genus includes several species. The most frequent enterococci recovered in clinical samples are *E. faecalis* and *E. faecium* but also *E. avium, E. casseliflavus, E. durans, E. gallinarum, E. hirae, E. mundtii* and *E. raffinosus* are occasionally encountered. Listed breakpoints have been largely developed using pre-clinical and clinical data on *E. faecalis* and *E. faecium*. The applicability of these breakpoints to other *Enterococcus* species is less certain as both clinical and pre-clinical data for these are mostly lacking. During 2023, in collaboration between EUCAST and experts in enterococci, data and breakpoints for other enterococci will be developed. Until then, use breakpoints below or the EUCAST Guidance Document on how to test and interpret results when there are no breakpoints.

- wenige präklinisch und klinische Daten für Enterokokken BP für *E. avium, E. casseliflavus, E.durans, E. gallinarium, E. hirae, E. mundtii, E. raffinosus*
- neue BP in Arbeit
- Verwendung aktueller Enterokokken BP oder Vorgehen wie bei Bakterien ohne BP

Einige „I“ Kategorien entfernt

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- ***Staphylococcus spp:*** Makrolide und Tetracyclin
- ***Streptococcus* group A, B,C, G**: Makrolide und Tetracyclin
- ***Streptococcus pneumoniae***: Cefpodoxim, Cefuroxim oral, Makrolide und Tetracyclin
- ***H. influenzae***: Doxycyclin
- ***Moraxella catarrhalis*:** Cefixim, Makrolide, Doxycyclin
- ***H. pylori*:** Clarithromycin
- ***N. gonorrhoeae*:** Tetracyclin
- ***Corynebacterium spp*.:** Rifampicin

~~*Pasteurella multocida*~~

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Tabelle gilt für *Pasteurella spp.*

EUCAST breakpoints are based mainly on data for Pasteurella multocida , although some data were included for other species (P. canis, P. dagmatis and P. aerogenes).

Corynebacterium spp.

– *Corynebacterium diphteriae* und *ulcerans* eigene BP

Corynebacterium diphtheriae* and *C. ulcerans **EUCAST Clinical Breakpoint Tables v. 13.1, valid from 2023-06-29**

Expert Rules and Expected Phenotypes
For abbreviations and explanations of breakpoints, see the Notes sheet

MIC determination (broth microdilution according to ISO standard 20776-1)
Medium: Mueller-Hinton broth + 5% lysed horse blood and 20 mg/L β-NAD (MH-F broth)
Inoculum: $5x10^5$ CFU/mL
Incubation: Sealed panels, air, 35±1°C, 18±2h. Isolates with insufficient growth after 16-20h incubation are reincubated immediately and MICs read after a total of 40-44h incubation.
Reading: Unless otherwise stated, read MICs at the lowest concentration of the agent that completely inhibits visible growth. See "EUCAST Reading Guide for broth microdilution" for further information.
Quality control: *Streptococcus pneumoniae* ATCC 49619. For agents not covered by this strain, see EUCAST QC Tables.

Disk diffusion (EUCAST standardised disk diffusion method)
Medium: Mueller-Hinton agar + 5% defibrinated horse blood and 20 mg/L β-NAD (MH-F)
Inoculum: McFarland 0.5
Incubation: 5% CO_2, 35±1°C, 18±2h. Isolates with insufficient growth after 16-20h incubation are reincubated immediately and inhibition zones read after a total of 40-44h incubation.
Reading: Unless otherwise stated, read zone edges as the point showing no growth viewed from the front of the plate with the lid removed and with reflected light. See "EUCAST Reading Guide for disk diffusion" for further information.
Quality control: *Streptococcus pneumoniae* ATCC 49619. For agents not covered by this strain, see EUCAST QC Tables.

Penicillins	MIC breakpoints (mg/L)			Disk content	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU	(µg)	S ≥	R <	ATU	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Benzylpenicillin	0.001	1		1 unit	50	12		**1/A.** Isolates "susceptible, increased exposure" (I) to benzylpenicillin can be reported susceptible to amoxicillin. Isolates resistant to benzylpenicillin should be tested for susceptibility to amoxicillin or reported resistant.
Amoxicillin	1[1]	1[1]			Note[A]	Note[A]		

Cephalosporins	MIC breakpoints (mg/L)			Disk content	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU	(µg)	S ≥	R <	ATU	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Cefotaxime	0.001[1]	2[1]		5	50[A]	15[A]		**1/A.** Susceptibility to cefotaxime can be inferred from benzylpenicillin.

Carbapenems	MIC breakpoints (mg/L)			Disk content	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU	(µg)	S ≥	R <	ATU	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Meropenem	0.25[1]	0.25[1]		10	24[A]	24[A]		**1/A.** Isolates "susceptible, increased exposure" (I) to benzylpenicillin can be reported susceptible to meropenem. Isolates resistant to benzylpenicillin should be tested for susceptibility to meropenem or reported resistant.

Fluoroquinolones	MIC breakpoints (mg/L)			Disk content	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU	(µg)	S ≥	R <	ATU	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Ciprofloxacin	0.001	0.5		5	50	24		

Anaerobier

Bacteroides spp., Prevotella spp., Fusobacterium necrophorum, Clostridium perfringens, Cutibacterium acnes, Clostridioides difficile

- Medium: Fastidious Anaerobe Agar + 5% defibrinated horse blood (FAA-HB)

- einige NEUE BP für **Ampicillin, Amoxicillin, Ampicillin/Sulbactam, Amoxicillin/ Clavulansäure, Ertapenem, Imipenem**

- *Cutibacterium acnes*: NEU **Cefotaxim, Ceftriaxon, Imipenem, Linezolid**

***Prevotella* spp.**

Antimicrobial agent
Benzylpenicillin
Ampicillin
Ampicillin-sulbactam
Amoxicillin
Amoxicillin-clavulanic acid
Piperacillin-tazobactam
Ertapenem
Imipenem
Meropenem
Clindamycin
Metronidazole

Anaerobier

Prevotella spp., Fusobacterium necrophorum, Clostridium perfringens, Cutibacterium acnes:

– gelistete Beta-Laktam AB können bei Empfindlichkeit von Benzylpenicillin abgeleitet werden (wenn R → testen)

Bacteroides spp.

– BP gelten auch für *Parabacteroides spp*. und *Phocaeicola dorei/vulgatus* (früher *Bacteroides dorei/vulgatus*)

Anaerobier

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Einschränkung bei *Prevotella spp*. und *Cutibacterium acnes*:

Beta-Laktam plus Inhibitor Kombinationen nur BP für Plättchendiffusion

***Prevotella* spp.**

Antimicrobial agent	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Benzylpenicillin	0.5[1]	0.5[1]		1 unit	20[A]	20[A]	
Ampicillin	0.5[1]	0.5[1]		2	25[A]	25[A]	
Ampicillin-sulbactam	Note[1,2]	Note[1,2]		10-10	33[A]	33[A]	
Amoxicillin	0.25[1]	0.25[1]			Note[A,B]	Note[A,B]	
Amoxicillin-clavulanic acid	Note[1,2]	Note[1,2]		2-1	24[A]	24[A]	
Piperacillin-tazobactam	Note[1,2]	Note[1,2]		30-6	26[A]	26[A]	

→ durch fixe Konzentrationen von Clavulansäure, Sulbactam und Tazobactam falsch niedrige MHKs

What to do when there are no breakpoints?

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1. Klinische Signifikanz?

2. Welche AB testen?

3. Mit welcher Methode testen?

Literatur, Wachstumscharakteristika



MHK Bestimmung

- **aerobe Bakterien**: Referenzmethode Boullion-Mikrodilution (MH, MH-F)
- **anaerobe Bakterien**: Agar Dilution (FAA-HB)
- Gradiententests (Herstellerangaben validiert für Spezies und AB)

What to do when there are no breakpoints?

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Vergleich mit Wildtypverteilung → (T)ECOFF

siehe EUCAST Tabelle Guidance Document (Aerobier/ Anaerobier)

MIC and zone diameter distributions and ECOFFs

1. EUCAST MIC and zone diameter distributions and ECOFFs
2. Correlation between MIC values and inhibition zone diameters

The EUCAST software, originally created in 2003, for displaying distributions of MIC-values (generated with methods calibrated to reference broth microdilution or for some agents and species, agar dilution) and inhibition zone diameters (generated with EUCAST standardised

Agents and notes for aerobic bacteria	MIC-values above which therapy with the agent should be discouraged	Notes
Benzylpenicillin	0.25	The value is valid unless beta-lactamase production is suspected.
Ampicillin, Amoxicillin, Ampicillin-sulbactam, Amoxicillin-clavulanic acid (IV only), Gram-negative organisms	2	If a beta-lactamase is detected, the value is only valid for amoxicillin-clavulanic acid and ampicillin-sulbactam.
Ampicillin, Amoxicillin, Ampicillin-sulbactam, Amoxicillin-clavulanic	0.5	If a beta-lactamase is detected, the value is only valid for amoxicillin-clavulanic acid and ampicillin-

What to do when there are no breakpoints?

Ordens klinikum Linz
Barmherzige Schwestern Elisabethinen

≤ (T)ECOFF/ MHK-Wert → **Kommentar**: z.B.: *„Nicht interpretierte Substanzen: eine formale Kategorisierung der Empfindlichkeit ist aktuell nicht möglich. Die erhobenen MHK-Werte legen nahe, dass eine Therapie mit den getesteten Substanzen möglich ist.“*

> (T)ECOFF/ MHK-Wert → **Kommentar, ggf. auch „R“**

keine „S“, „I“, („R“) – Bewertung

Aerobe Bakterien ohne BP

Table 1. Antimicrobial agents relevant for the treatment of aerobic bacteria with guidance to exclude resistance in bacteria lacking breakpoints in standard EUCAST breakpoint tables.
Determine an MIC and compare with numerical values to exclude resistance. The clinical use of agents for which MIC-values are higher than those listed should be discouraged and the use of agents for which the MIC is the same or lower can be cautiously encouraged. Avoid reporting isolates S, I or R - instead add a comment to discourage or encourage therapy. The proposed values are based on (i) a compromise between current EUCAST susceptible (S or I) breakpoints for species already in the tables, (ii) wild type distributions for microorganisms when available and (iii) the PK/PD breakpoint.

Agents and notes for aerobic bacteria	MIC-values above which therapy with the agent should be discouraged	Notes
Benzylpenicillin	0.25	The value is valid unless beta-lactamase production is suspected.
Ampicillin, Amoxicillin, Ampicillin-sulbactam, Amoxicillin-clavulanic acid (IV only), Gram-negative organisms	2	If a beta-lactamase is detected, the value is c… valid for amoxicillin-clavulanic acid and ampi… sulbactam.
Ampicillin, Amoxicillin, Ampicillin-sulbactam, Amoxicillin-clavulanic acid (IV only), Gram-positive organisms	0.5	If a beta-lactamase is detected, the value is c… valid for amoxicillin-clavulanic acid and ampi… sulbactam.
Piperacillin-tazobactam, Gram-negative organisms	2	The piperacillin-tazobactam breakpoint is conservative and on par with the aminopeni… breakpoints
Cefotaxime	0.25	Cefotaxime and ceftriaxone – resistance to e… excludes the use of both.
Ceftriaxone	0.25	Cefotaxime and ceftriaxone – resistance to e… excludes the use of both.



PK-PD (Non-species related) breakpoints
For abbreviations and explanations of breakpoints, see the Notes sheet

These breakpoints are used only when there are no species-specific breakpoints or other recommendati
If the MIC is greater than the PK-PD resistant breakpoint, advise against use of the agent.
If the MIC is less than or equal to the PK-PD susceptible breakpoint, suggest that the agent can be used with ca
based on PK-PD breakpoints only, and include the dosage on which PK-PD breakpoint is based.
More information is available in the EUCAST Guidance Document on how to test and interpret results wh

Penicillins	MIC breakpoints (mg/L)		Notes
	S ≤	R >	
Benzylpenicillin	0.25	2	1. For susceptibility testin
Ampicillin	2	8	2. For susceptibility testin
Ampicillin-sulbactam	2[1]	8[1]	3. For susceptibility testin
Amoxicillin	2	8	
Amoxicillin-clavulanic acid	2[2]	8[2]	
peracillin	8	16	
peracillin-tazobactam	8[3]	16[3]	
~~carcillin~~			
carcillin-clavulanic acid	8[2]	16[2]	
mocillin	8	8	
henoxymethylpenicillin	IE	IE	
xacillin	IE	IE	
loxacillin	IE	IE	
icloxacillin	IE	IE	
ucloxacillin	IE	IE	
ecillinam oral (pivmecillinam) ncomplicated UTI only)	IE	IE	

Eucast News and Updates 30.09.23

Plan: PK/PD entfernen → Consultation

RAST

E. coli* und *K. pneumoniae (inkl. ***K. variicola, quasipneumoniae***):

– NEU BP für Ampicillin, Amoxicillin/ Clavulansäure, Temocillin, Imipenem-Relebactam, Meropenem-Vaborbactam (4,6,8,16-20h)

P. aeruginosa:

– NEU BP: für Imipenem-Relebactam, Meropenem-Vaborbactam (6,8,16-20h)

Aminoglykoside: BP in brackets

BP NEU **für 16-20h** für ***Acinetobacter baumannii, E. faecalis, E. faecium***

Status quo Fosfomycin i.v.

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- *Pseudomonas spp*.
  - ECOFF geändert: 265 mg/L

- 2022 und 2023 (bis 09/2023) Consultation

The new breakpoints will read as follows:

Species	Current MIC Breakpoints (mg/L)		Species	Proposed MIC Breakpoints (mg/L)	
	S ≤	R >		S ≤	R >
Enterobacterales	8	8	*E. coli*	8	8
			K. pneumoniae	Note[1]	Note[1]
			Enterobacterales except *E. coli* and *K. pneumoniae*	IE[2]	IE[2]
P. aeruginosa	Note[3]	Note[3]	*P. aeruginosa*	Note[3]	Note[3]
Acinetobacter spp.	-	-	*Acinetobacter* spp.	-	
S. aureus	32	32	*S. aureus*	~~(32)~~ Note[4]	~~(32)~~ Note[4]
Enterococcus spp.	-	-	*Enterococcus* spp.	Note[5]	Note[5]
Notes [3]Agar Dilution is the reference method for fosfomycin. MICs must be determined in the presence of glucose-6-phosphate (25 mg/L in the medium. The ECOFF is 256 mg/L.			**Notes** [1]The ECOFF of 128 mg/L is not predictive of efficacy irrespective of whether the agent is used alone or in combination [2]For other *Enterobacterales* there is both insufficient clinical data and MIC-data to define either a clinical breakpoint or an ECOFF. [3]The ECOFF of 256 mg/L is not predictive of efficacy irrespective of whether the agent is used alone or in combination. [4]The ECOFF of 32 mg/L is not predictive of efficacy irrespective of whether the agent is used alone or in combination. [5]The ECOFF of 128 mg/L is not predictive of efficacy irrespective of whether the agent is used alone or in combination.		

Status quo Cefiderocol

13 Sep 2023: Cefiderocol susceptibility testing - an update

Evaluierung on-going → Ende Oktober/ November Ergebnisse zu erwarten

→ voraussichtlich ATU kleiner (derzeit *Enterobacterales*: ATU 18-22mm)

bis dahin weiterhin WARNUNG:

– kommerzielle Gradientendiffusionstest und andere Tests weitherhin problematisch → Plättchendiffusion empfohlen
– Vorsicht bei der Wahl bestimmter Agarmedien und Discs

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Vielen Dank für Ihre Aufmerksamkeit!



Dosages used to define breakpoints

EUCAST Clinical Breakpoint Tables v. 13.1, valid from 2023-06-29

EUCAST breakpoints are based on the following dosages (see section 8 in Rationale Documents). 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.

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.

Penicillins	Standard dosage	High dosage	Uncomplicated UTI	Special situations
Benzylpenicillin	0.6 g (1 MU) x 4 iv	1.2 g (2 MU) x 4-6 iv		**Meningitis caused by *S. pneumoniae:*** For a dose of 2.4 g (4 MU) x 6 iv, isolates with MIC ≤0.06 mg/L are susceptible. **Pneumonia caused by *S. pneumoniae:* breakpoints are related to dosage:** For a dose of 1.2 g (2 MU) x 4 iv, isolates with MIC ≤ 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 ≤1 mg/L are susceptible. For a dose of 2.4 g (4 MU) x 6 iv, isolates with MIC ≤2 mg/L are susceptible.
Ampicillin	2 g x 3 iv	2 g x 4 iv		**Meningitis:** 2 g x 6 iv
Ampicillin-sulbactam iv	(2 g ampicillin + 1 g sulbactam) x 3 iv	(2 g ampicillin + 1 g sulbactam) x 4 iv		
Ampicillin-sulbactam oral	None	None	0.75 g x 2 oral	
Amoxicillin iv	1 g x 3-4 iv	2 g x 6 iv		**Meningitis:** 2 g x 6 iv
Amoxicillin oral	0.5 g x 3 oral	0.75-1 g x 3 oral	0.5 g x 3 oral	
Amoxicillin-clavulanic acid iv	(1 g amoxicillin + 0.2 g clavulanic acid) x 3-4 iv	(2 g amoxicillin + 0.2 g clavulanic acid) x 3 iv		
Amoxicillin-clavulanic acid oral	(0.5 g amoxicillin + 0.125 g clavulanic acid) x 3 oral	(0.875 g amoxicillin + 0.125 g clavulanic acid) x 3 oral	(0.5 g amoxicillin + 0.125 g clavulanic acid) x 3 oral	Amoxicillin-clavulanic acid has separate breakpoints for systemic infections and uncomplicated UTI. When amoxicillin-clavulanic acid is reported for uncomplicated UTI, the report must make clear that the susceptibility category is only valid for uncomplicated UTI.