

Aplicando os novos pontos de corte em casos clínicos

Meningite por *S.pneumoniae* Com reportar meu laudo

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Most common causative pathogens in neonatal meningitis are *Streptococcus agalactiae* and *Escherichia coli*.

Most common causative pathogens in children beyond the neonatal age are *Neisseria meningitidis* and *Streptococcus pneumoniae*.

Most common causative pathogens in adults are *Streptococcus pneumoniae* and *Neisseria meningitidis*. Another important causative microorganism in adults is *Listeria monocytogenes*.

ESCMID guideline: diagnosis and treatment of acute bacterial meningitis

D. van de Beek¹, C. Cabellos², O. Dzunpova³, S. Esposito⁴, M. Klein⁵, A. T. Kloek¹, S. L. Leib⁶, B. Mourvillier⁷, C. Ostergaard⁸, P. Pagliano⁹, H. W. Pfister⁵, R. C. Read¹⁰, O. Resat Sipahi¹¹ and M. C. Brouwer¹, for the ESCMID Study Group for Infections of the Brain (ESGIB)

TABLE 4.1. Empiric antibiotic in-hospital treatment for community-acquired bacterial meningitis [3]

Patient group	Standard treatment		Intravenous dose ^a
	Reduced <i>Streptococcus pneumoniae</i> antimicrobial sensitivity to penicillin	<i>S. pneumoniae</i> susceptible to penicillin	
Neonates <1 month old	Amoxicillin/ampicillin/penicillin plus cefotaxime, or amoxicillin/ampicillin plus an aminoglycoside		Age <1 week: cefotaxime 50 mg/kg q8h; ampicillin/amoxicillin 50 mg/kg q8h; gentamicin 2.5 mg/kg q12h Age 1–4 weeks: ampicillin 50 mg/kg q6h; cefotaxime 50mg/kg q6–8h; gentamicin 2.5 mg/kg q8h; tobramycin 2.5 mg/kg q8h; amikacin 10 mg/kg q8h
Age 1 month to 18 years	Cefotaxime or ceftriaxone plus vancomycin or rifampicin	Cefotaxime or ceftriaxone	Vancomycin 10–15 mg/kg q6h to achieve serum trough concentrations of 15–20 µg/mL; rifampicin 10 mg/kg q12h up to 600 mg/day; cefotaxime 75 mg/kg q6–8h; ceftriaxone 50 mg/kg q12h (maximum 2 g q12h)
Age >18 and <50 years	Cefotaxime or ceftriaxone plus vancomycin or rifampicin	Cefotaxime or ceftriaxone	Ceftriaxone 2 g q12h or 4 g q24h; cefotaxime 2 g q4–6 h; vancomycin 10–20 mg/kg q8–12h to achieve serum trough concentrations of 15–20 µg/mL; rifampicin 300 mg q12h
Age >50 years, or Age >18 and <50 years plus risk factors for <i>Listeria monocytogenes</i> ^a	Cefotaxime or ceftriaxone plus vancomycin or rifampicin plus amoxicillin/ampicillin/penicillin G	Cefotaxime or ceftriaxone plus amoxicillin/ampicillin/penicillin G	Ceftriaxone 2 g q12h or 4 g q24h; cefotaxime 2 g q4–6h; vancomycin 10–20 mg/kg q8–12h to achieve serum trough concentrations of 15–20 µg/mL; rifampicin 300 mg q12h, amoxicillin or ampicillin 2 g q4h

^aDiabetes mellitus, use of immunosuppressive drugs, cancer and other conditions causing immunocompromise.

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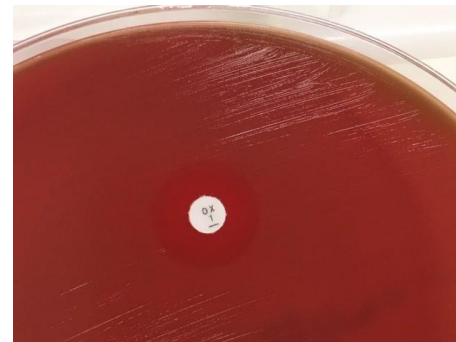
TABLE 4.2. Specific antibiotic in-hospital treatment for community-acquired bacterial meningitis^a

Microorganism	Standard treatment	Alternatives	Duration
<i>Streptococcus pneumoniae</i>			
Penicillin susceptible	Penicillin or amoxicillin/ampicillin	Ceftriaxone, cefotaxime, chloramphenicol	10–14 days
Penicillin resistant third-generation cephalosporin susceptible	Ceftriaxone or cefotaxime	Cefepime, meropenem, moxifloxacin ^b	10–14 days
Cephalosporin resistant	Vancomycin <i>plus</i> rifampicin, or vancomycin <i>plus</i> ceftriaxone or cefotaxime, or rifampicin <i>plus</i> ceftriaxone or cefotaxime ^c	Vancomycin <i>plus</i> moxifloxacin, ^b linezolid	10–14 days

Cefalosporinas de 3^a geração, Vancomicina, Meropenem

Teste de suscetibilidade aos beta-lactâmicos

- Triagem com disco Oxacilina 1 µg: MH-F (5% de sangue desfibrinado de cavalo + 20mg/L β-NAD).
 - Suspensão bacteriana – 0,5 de McFarland (1 a 2 x 10⁸ UFC/mL).
 - *S. pneumoniae* (ágar chocolate): 1.0 de McFarland.
 - Incubação: 5% CO₂, 35 ± 1°C, 18 ± 2h
 - Leitura do diâmetro do halo



- Triagem com determinação de CIM Benzilpenicilina.

Screening for beta-lactam resistance in *S. pneumoniae*

Oxacillin 1 µg disk test or benzylpenicillin MIC

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

Oxacillin zone diameter ≥ 20 mm or
benzylpenicillin MIC ≤ 0.06 mg/L
Excludes all beta-lactam resistance mechanisms

Oxacillin zone diameter < 20 mm* or
benzylpenicillin MIC > 0.06 mg/L*
Beta-lactam resistance mechanism detected

Report susceptible (S) to any beta-lactam agents for which clinical breakpoints are available, including those with "Note", except for cefactor, which if reported, should be reported "susceptible, increased exposure" (I)

Benzylpenicillin
(meningitis)
and
phenoxymethylpenicillin
(all indications)

Report resistant (R)

Benzylpenicillin
(indications other than
meningitis)

Determine the MIC and
interpret according to the
clinical breakpoints

Ampicillin, amoxicillin and piperacillin
(without and with
beta-lactamase inhibitor),
cefepime, cefotaxime, ceftaroline,
ceftolizole and ceftriaxone

Oxacillin
zone ≥ 8 mm

Report susceptible
(S)

Oxacillin zone
 < 8 mm

For intravenous ampicillin, amoxicillin and
piperacillin (without and with inhibitor),
infer susceptibility from ampicillin

For oral amoxicillin (without
and with inhibitor), see
breakpoint recommendations

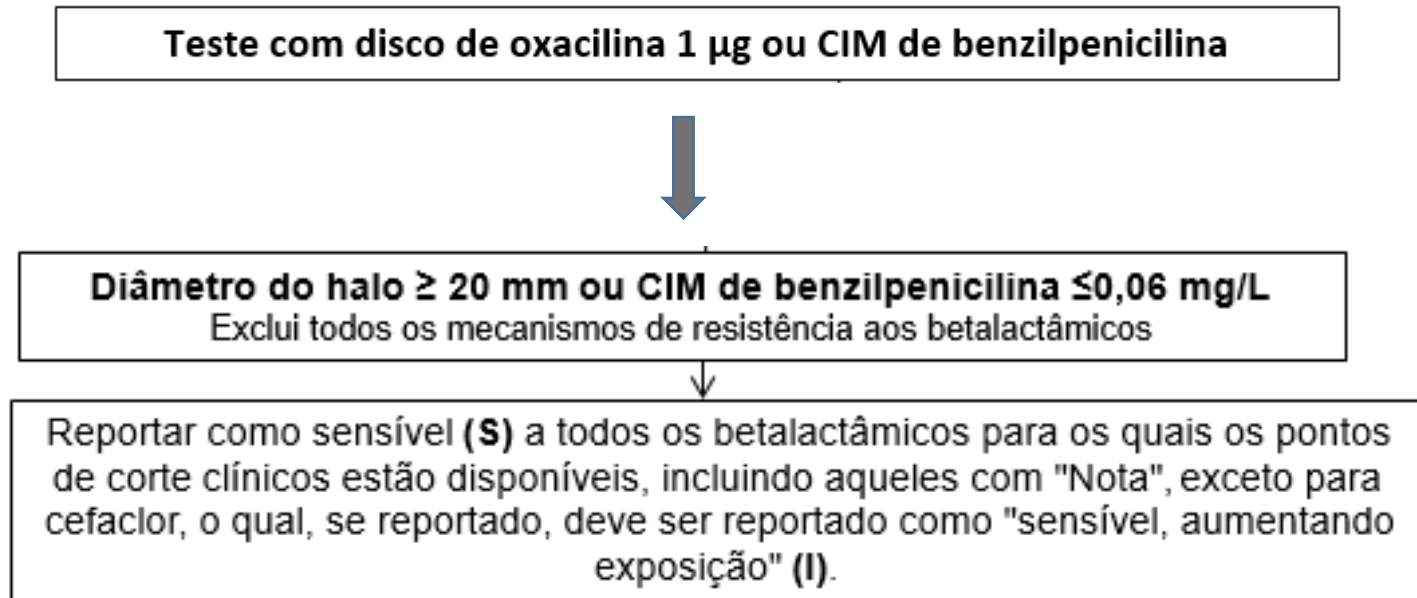
For cefepime, cefotaxime, ceftaroline, ceftolizole and
ceftriaxone,
determine the MIC and interpret according to the clinical breakpoints

**Other beta-
lactam agents**

Determine the MIC and
interpret according to the
clinical breakpoints

* In meningitis confirm by determining the MIC for the agent considered for clinical use.

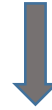
Triagem de resistência aos beta-lactâmicos em *S.pneumoniae*



Benzilpenicilina, Ampicilina, Amoxicilina, Cefotaxima,
Ceftriaxona, Meropenem

Triagem de resistência aos beta-lactâmicos em *S.pneumoniae*

Teste com disco de oxacilina 1 µg ou CIM de benzilpenicilina



Diâmetro do halo < 20 mm* ou CIM de benzilpenicilina > 0,06 mg/L *
Mecanismo de resistência a betalactâmicos detectado

Benzilpenicilina
(meningite)
e
fenoximetilpenicilina
(todas as indicações)

Reportar resistente (**R**)

Benzilpenicilina
(infecções não meningéas)

Determinar a CIM e interpretar de acordo com os pontos de corte clínicos

Ampicilina, amoxicilina e piperacilina
(com e sem inibidor de betalactamases), cefepima, cefotaxima, ceftarolina, ceftobiprole e ceftriaxona

Avaliar diâmetro do halo de Oxacilina

Outros agentes betalactâmicos

Determinar a CIM e interpretar de acordo com os pontos de corte clínicos

* Em meningite, confirmar o resultado determinando a CIM para os agentes considerados para uso clínico.

Penicillins ¹	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Benzylicillin (indications other than meningitis) ²	0.06 ¹	2 ¹			Note ^A	Note ^A	
Benzylicillin (meningitis)	0.06 ¹	0.06 ¹			Note ^A	Note ^A	
Ampicillin (indications other than meningitis)	0.5 ¹	2 ¹		2	22 ^A	16 ^A	
Ampicillin (meningitis)	0.5 ¹	0.5 ¹			Note ^{A,B}	Note ^{A,B}	
Ampicillin-sulbactam ³	Note ^{1,4}	Note ^{1,4}			Note ^{A,C}	Note ^{A,C}	
Amoxicillin iv (indications other than meningitis)	Note ^{1,4}	Note ^{1,4}			Note ^{A,C}	Note ^{A,C}	
Amoxicillin iv (meningitis)	0.5 ¹	0.5 ¹			Note ^{A,B}	Note ^{A,B}	
Amoxicillin oral	0.5 ¹	1 ¹			Note ^{A,D}	Note ^{A,D}	
Amoxicillin-clavulanic acid iv ³	Note ^{1,4}	Note ^{1,4}			Note ^{A,C}	Note ^{A,C}	
Amoxicillin-clavulanic acid oral ³	0.5 ^{1,5}	1 ^{1,5}			Note ^{A,D}	Note ^{A,D}	
Piperacillin	Note ^{1,4}	Note ^{1,4}			Note ^{A,C}	Note ^{A,C}	
Piperacillin-tazobactam ³	Note ^{1,4}	Note ^{1,4}			Note ^{A,C}	Note ^{A,C}	
Ticarcillin	-	-			-	-	
Ticarcillin-clavulanic acid	-	-			-	-	
Temocillin	-	-			-	-	
Phenoxymethylpenicillin	Note ¹	Note ¹			Note ^A	Note ^A	
Oxacillin (screen only)	NA	NA		1	20 ^E	Note ^E	
Cloxacillin	-	-			-	-	
Dicloxacillin	-	-			-	-	
Flucloxacillin	-	-			-	-	
Mecillinam oral (pivmecillinam) (uncomplicated UTI only)	-	-			-	-	

Cephalosporins ¹	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Cefaclor	0.001	0.5		30	50	28	
Cefadroxil	-	-			-	-	
Cefalexin	-	-			-	-	
Cefazolin	-	-			-	-	
Cefepime	1	2			Note ^A	Note ^A	
Cefiderocol	IE	IE			IE	IE	
Cefixime	-	-			-	-	
Cefotaxime (indications other than meningitis)	0.5	2			Note ^A	Note ^A	
Cefotaxime (meningitis)	0.5	0.5			Note ^{A,B}	Note ^{A,B}	
Cefoxitin	IE	IE			IE	IE	
Cefpodoxime	0.25	0.5			Note ^A	Note ^A	
Ceftaroline	0.25	0.25			Note ^A	Note ^A	
Ceftazidime	-	-			-	-	
Ceftazidime-avibactam	-	-			-	-	
Ceftibuten	-	-			-	-	
Ceftobiprole	0.5	0.5			Note ^A	Note ^A	
Ceftolozane-tazobactam	-	-			-	-	
Ceftriaxone (indications other than meningitis)	0.5	2			Note ^A	Note ^A	
Ceftriaxone (meningitis)	0.5	0.5			Note ^{A,B}	Note ^{A,B}	
Cefuroxime iv	0.5	1			Note ^A	Note ^A	
Cefuroxime oral	0.25	0.5			Note ^A	Note ^A	

Carbapenems ^{1,2}	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Doripenem	1	1			Note ^A	Note ^A	
Ertapenem	0.5	0.5			Note ^A	Note ^A	
Imipenem	2	2			Note ^A	Note ^A	
Imipenem-relebactam³	Note ³	Note ³			Note ^B	Note ^B	
Meropenem (indications other than meningitis)	2	2			Note ^A	Note ^A	
Meropenem (meningitis)	0.25	0.25			Note ^{A,C}	Note ^{A,C}	
Meropenem-vaborbactam³	Note ³	Note ³			Note ^B	Note ^B	

Triagem de resistência aos beta-lactâmicos em *S.pneumoniae*

Teste com disco de oxacilina 1 µg ou CIM de benzilpenicilina

Diâmetro do halo < 20 mm* ou CIM de benzilpenicilina > 0,06 mg/L *
Mecanismo de resistência a betalactâmicos detectado

Ver alerta BrCAST-EUCAST sobre o teste de benzilpenicilina e gradiente de difusão
* <http://www.eucast.org/warnings/>.

Benzilpenicilina
(meningite)
e
fenoximetilpenicilina
(todas as indicações)

Reportar resistente (R)

Benzilpenicilina *
(infecções não meningeas)

Determinar a CIM e interpretar de acordo com os pontos de corte clínicos

Ampicilina, amoxicilina e piperacilina
(com e sem inibidor de betalactamases), **cefepima, cefotaxima, ceftarolina, ceftobiprole e ceftriaxona**

Diâmetro do halo de oxacilina ≥ 8 mm

Reportar sensível (S)*

Diâmetro do halo de oxacilina < 8 mm

Outros agentes betalactâmicos

Determinar a CIM e interpretar de acordo com os pontos de corte clínicos

Para ampicilina, amoxicilina e piperacilina (sem e com inibidor) intravenosas inferir a sensibilidade a partir da ampicilina

Para amoxicilina oral (sem e com inibidor) ver recomendações de ponto de corte

Para cefepima, cefotaxima, ceftarolina, ceftobiprole e ceftriaxona determinar a CIM e interpretar de acordo com os pontos de corte clínicos

Glycopeptides and lipoglycopeptides	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Dalbavancin	IE	IE			IE	IE	
Oritavancin	IE	IE			IE	IE	
Teicoplanin ¹	2	2		30	17 ^A	17 ^A	
Telavancin	IE	IE			IE	IE	
Vancomycin ¹	2	2		5	16 ^A	16 ^A	

Possibilidades para testar/reportar no laudo

- ✓ Cefotaxima
- ✓ Ceftriaxona
- ✓ Vancomicina
- ✓ Meropenem
- ✓ Benzilpenicilina
- ✓ Ampicilina
- ✓ Amoxicilina

- Cloranfenicol
- Rifampicina

Miscellaneous agents	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Chloramphenicol ¹	8	8		30	21	21	
Colistin	-	-			-	-	
Daptomycin	IE	IE			IE	IE	
Fosfomicin iv	IE	IE			IE	IE	
Fosfomicin oral	-	-			-	-	
Fusidic acid	-	-			-	-	
Lefamulin	0.5	0.5		5	12	12	
Metronidazole	-	-			-	-	
Nitrofurantoin (uncomplicated UTI only)	-	-			-	-	
Nitroxoline (uncomplicated UTI only)	-	-			-	-	
Rifampicin	0.125	0.5		5	22	17	
Spectinomycin	-	-			-	-	
Trimethoprim (uncomplicated UTI only)	-	-			-	-	
Trimethoprim-sulfamethoxazole ²	1	2		1.25-23.75	13	10	

Observações em relatos de casos

- Moxifloxacina
- Linezolida



Não reportar
rotineiramente

Fluoroquinolones	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Ciprofloxacin	-	-			-	-	
Delafloxacin	IE	IE			IE	IE	
Levofloxacin	0.001	2		5	50 ^A	16 ^A	
Moxifloxacin	0.5	0.5		5	22 ^A	22 ^A	
Nalidixic acid (screen only)	NA	NA			NA	NA	
Norfloxacin (screen only)	NA	NA		10	10 ^B	Note ^B	
Ofloxacin	-	-			-	-	

Oxazolidinones	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Linezolid	2	2		10	22	22	
Tedizolid	IE	IE			IE	IE	

Antibióticos com pontos de corte clínicos que não devem ser reportados nos laudos

- Macrolídeos
- Clindamicina
- Tetraciclina
- Levofloxacina
- Cefalosporinas de segunda geração
- Teicoplanina

Obrigada!