Veranderingen in EUCAST 2022

Anouk Muller
Arts-microbioloog
HaaglandenMC, Den Haag
ErasmusMC, Rotterdam

24-01-2022
WAMM

Inhoud presentatie

- Doseringstabel
- Antibacteriële middelen
  - “BP in Brackets”
  - Aparte screeningsbreekpunten
  - DD voor anaeroben
  - Nieuwe breekpunten
- Antifungale middelen

Doseringen

- Opmerking geplaatst “The high exposure dosing regimen pertains to the severity of the infection or drug exposure at the site of infection”
  - Oxacilline
  - Cloxacilline
  - Dicloxacilline
  - Flucloxacilline
  - Clindamycine
- Rifampicine: hoge dosering is verwijderd (alleen 600mg 1dd)

“breakpoints in brackets”

- Onderscheid tussen isolaten met en zonder fenotypisch detecteerbaar resistentie mechanisme.
- Gebaseerd op ECOFF
- Indien meerdere species in 1 groep, dan ‘best fit’ ECOFF.
- Geen klinisch bewijs dat monotherapie effectief is
- Meestal gegeven in combinatie met ander antibioticum

“breakpoints in brackets”

Groep	Antibioticum
Enterobacterales	Colistine
Pseudomonas	Colistine
Acinetobacter	Colistine
Stafylokokken	Aminoglycosiden
Bacteroides	clindamycine
Reeds in tabel 2021	
Enterobacterales	Amikacine, tobramycine en gentamicine
Pseudomonas	Amikacine en tobramycine

Aparte screeningsbreekpunten

- Screeningstest gebruikt 1 antibioticum om resistentie tegen een of middelen van dezelfde klasse te voorspellen.
- Vaak gevoeliger en/of robuster dan het testen van een individueel middel
- Minder testen nodig

Algemene interpretatie

- Negative screening test:
  - MIC below or equal to or zone diameter above or equal to the susceptible breakpoint for the screening agent. No resistance mechanisms to the antimicrobial class detected.
- Positive screening test:
  - MIC above or zone diameter below the resistant breakpoint for the screening agent. Resistance mechanisms to the antimicrobial class detected.

Instructies om te handelen bij individuele testen staat bij de 'Note' van de betreffende test.

Aparte screeningsbreekpunten

groep	Screening
Stafylokokken	Erytromycine
Stafylokokken	Tetracycline
Streptokokken A,B,C,G	Tetracycline
Pneumokokken	Tetracycline
Burkholderia pseudomallei	Tetracycline

Voorbeeld screeningsbreekpunt

***Staphylococcus* spp.**

Expert Rules and Intrinsic Resistance Tables

Macrolides, lincosamides and streptogramins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Azithromycin	2[1]	2[1]			Note[A]	Note[A]	
Clarithromycin	1[1]	2[1]			Note[A]	Note[A]	
Erythromycin	1	2		15	21	18	
Erythromycin (screen only)	1[1]	1[1]		15	21[A]	21[A]	

Getallen anders!!

- 1/A. Erythromycin can be used to screen for macrolide resistance in staphylococci. Isolates categorised as **screen negative** can be reported **susceptible to azithromycin, clarithromycin and roxithromycin**. Isolates categorised as **screen positive** should be **tested for susceptibility to individual agents or reported resistant**.

Disk diffusie voor anaeroben

- Gedetailleerde info: seminar van de EUCAST van 9 december 2021 (beschikbaar via EUCAST website)
- Project loopt nog
- Nu informatie beschikbaar over 5 species en een beperkt aantal antibiotica
- In de loop van 2022 volgen voor deze species meer antibiotica
- Daarna andere species en andere incubatietijden

Momenteel beschikbaar

Species and antimicrobial agents

- 5 commonly isolated anaerobic bacteria
  - *Bacteroides* spp.
  - *Prevotella* spp.
  - *Fusobacterium necrophorum*
  - *Clostridium perfringens*
  - *Cutibacterium acnes*
- Clinically relevant antimicrobial agents
  - Benzylpenicillin 1 unit
  - Piperacillin-tazobactam 30-6 µg
  - Meropenem 10 µg
  - Vancomycin 5 µg
  - Clindamycin 2 µg
  - Metronidazole 5 µg

Dia van EUCAST seminar 9-12-2021

De methode in het kort

Disk diffusion methodology

- **Medium:** Fastidious Anaerobe Agar (FAA) with 5% mechanically defibrinated horse blood
  - Agar depth 4.0 ± 0.5 mm
  - Plates must be dried prior to inoculation
- **Inoculum:** McF 1.0 (overnight culture from non-selective media)
- **Incubation:** Anaerobic environment 35-37°C for 16-20 h

Dia van EUCAST seminar 9-12-2021

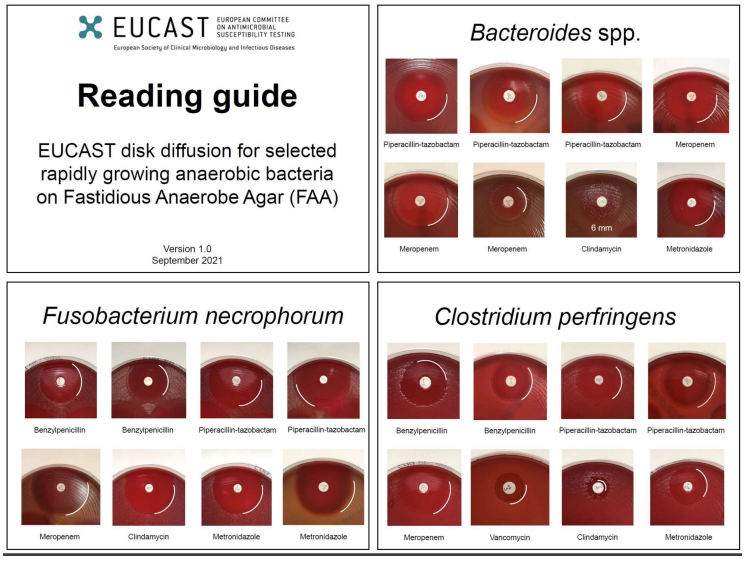
Methode (2)

Streaking of plates and application of disks

- For *Bacteroides* spp., remove excess fluid by turning the swab against the inside of the tube to avoid over-inoculation.
- Spread the inoculum evenly over the entire agar surface, ensuring that there are no gaps between streaks.
  - This is particularly important for *Cutibacterium acnes*, which grows with small colonies and poor contrast to the FAA media.
- Limit the number of disks on each plate to allow good growth and to avoid overlapping of zones.

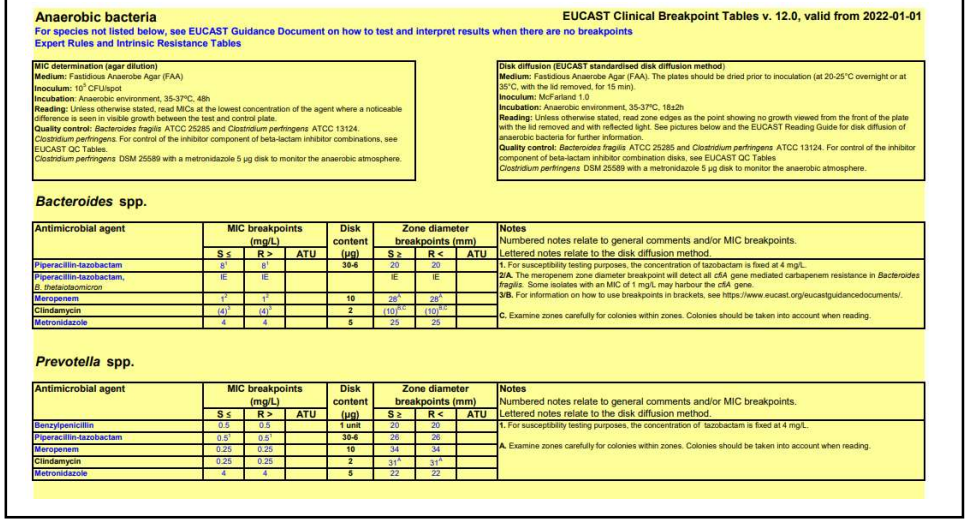
Dia van EUCAST seminar 9-12-2021

Hulp bij het aflezen van de zones



Dia van EUCAST seminar 9-12-2021

Voorbeeld uit breekpuntentabel 2022



Anaerobic bacteria — **EUCAST Clinical Breakpoint Tables v. 12.0, valid from 2022-01-01**

For species not listed below, see EUCAST Guidance Document on how to test and interpret results when there are no breakpoints
Expert Rules and Intrinsic Resistance Tables

MIC determination (agar dilution)
Medium: Fastidious Anaerobe Agar (FAA)
Inoculum: 10^5 CFU/spot
Incubation: Anaerobic environment, 35-37°C, 48h
Reading: Unless otherwise stated, read MICs at the lowest concentration of the agent where a noticeable difference is seen in visible growth between the test and control plate.
Quality control: *Bacteroides fragilis* ATCC 25285 and *Clostridium perfringens* ATCC 13124.
Clostridium perfringens. For control of the inhibitor component of beta-lactam inhibitor combinations, see EUCAST QC Tables.
Clostridium perfringens DSM 25589 with a metronidazole 5 µg disk to monitor the anaerobic atmosphere.

Disk diffusion (EUCAST standardised disk diffusion method)
Medium: Fastidious Anaerobe Agar (FAA). The plates should be dried prior to inoculation (at 20-25°C overnight or at 35°C, with the lid removed, for 15 min).
Inoculum: McFarland 1.0
Incubation: Anaerobic environment, 35-37°C, 18±2h
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 pictures below and the EUCAST Reading Guide for disk diffusion of anaerobic bacteria for further information.
Quality control: *Bacteroides fragilis* ATCC 25285 and *Clostridium perfringens* ATCC 13124. For control of the inhibitor component of beta-lactam inhibitor combination disks, see EUCAST QC Tables
Clostridium perfringens DSM 25589 with a metronidazole 5 µg disk to monitor the anaerobic atmosphere.

***Bacteroides* spp.**

Antimicrobial agent	MIC breakpoints (mg/L) S ≤	R >	ATU	Disk content (µg)	Zone diameter breakpoints (mm) S ≥	R <	ATU
Piperacillin-tazobactam	8[1]	8[1]		30-6	20	20	
Piperacillin-tazobactam, *B. thetaiotaomicron*	IE	IE			IE	IE	
Meropenem	1[2]	1[2]		10	26[A]	26[A]	
Clindamycin	(4)[3]	(4)[3]		2	(10)[B,C]	(10)[B,C]	
Metronidazole	4	4		5	25	25	

Notes
Numbered notes relate to general comments and/or MIC breakpoints.
Lettered notes relate to the disk diffusion method.
1. For susceptibility testing purposes, the concentration of tazobactam is fixed at 4 mg/L.
2/A. The meropenem zone diameter breakpoint will detect all *cfiA* gene mediated carbapenem resistance in *Bacteroides fragilis*. Some isolates with an MIC of 1 mg/L may harbour the *cfiA* gene.
3/B. For information on how to use breakpoints in brackets, see https://www.eucast.org/eucastguidancedocuments/.
C. Examine zones carefully for colonies within zones. Colonies should be taken into account when reading.

***Prevotella* spp.**

Antimicrobial agent	MIC breakpoints (mg/L) S ≤	R >	ATU	Disk content (µg)	Zone diameter breakpoints (mm) S ≥	R <	ATU
Benzylpenicillin	0.5	0.5		1 unit	20	20	
Piperacillin-tazobactam	0.5[1]	0.5[1]		30-6	26	26	
Meropenem	0.25	0.25		10	34	34	
Clindamycin	0.25	0.25		2	31[A]	31[A]	
Metronidazole	4	4		5	22	22	

Notes
Numbered notes relate to general comments and/or MIC breakpoints.
Lettered notes relate to the disk diffusion method.
1. For susceptibility testing purposes, the concentration of tazobactam is fixed at 4 mg/L.
A. Examine zones carefully for colonies within zones. Colonies should be taken into account when reading.

Nieuwe breekpunten

- Meropenem/vaborbactam DD
  - Enterobacterales
  - Pseudomonas
- Meropenem-non-meningitis: apart breekpunt voor Pseudomonas non-aeruginosa
- *S aureus* en Delafloxacin: apart breekpunt voor CAP en een ander voor huidinfecties
- *Vibrio spp*
- PK/PD breakpoint: temocilline toegevoegd (en oritavancin verwijderd)
- anaeroben

Andere veranderingen

- Waarden in verschillende breekpunten
- Tekstuele veranderingen
- Schema's pneumokokken en haemophilus

Voorbeeld bij pneumokokken

Penicillins[1]	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Benzylpenicillin (indications other than meningitis)[2]	0.06	2			Note[A]	Note[A]	
Benzylpenicillin (meningitis)	0.06	0.06			Note[A]	Note[A]	
Ampicillin (indications other than meningitis)	0.5	1		2	22	19	
Rifampicin	0.125	0.125		5	22	22	

Oud: 2

Oud: 16

Oud: 0.5

Oud: 17

Erasmus MC Universitair Medisch Centrum Rotterdam Zafung

SWAB Stichting Werkgroep Antibioticabeleid

H+ MC

Stafylokokken

Penicillins[1]	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Benzylpenicillin, *S. aureus*	0.125[1]	0.125[1]		1 unit	26[A,B]	26[A,B]	
Benzylpenicillin, *S. lugdunensis*	0.125	0.125		1 unit	26	26	
Benzylpenicillin, other staphylococci	Note[2]	Note[2]			Note[C]	Note[C]	
Ampicillin, *S. saprophyticus*	Note[2,3]	Note[2,3]		2	18[C,D]	18[C,D]	
Ampicillin-sulbactam	Note[1,2,3]	Note[1,2,3]			Note[A,C,D]	Note[A,C,D]	
Amoxicillin	Note[1,2,3]	Note[1,2,3]			Note[A,C,D]	Note[A,C,D]	
Amoxicillin-clavulanic acid	Note[1,2,3]	Note[1,2,3]			Note[A,C,D]	Note[A,C,D]	
Piperacillin	Note[1,2,3]	Note[1,2,3]			Note[A,C,D]	Note[A,C,D]	
Piperacillin-tazobactam	Note[1,2,3]	Note[1,2,3]			Note[A,C,D]	Note[A,C,D]	
Ticarcillin	Note[1,2]	Note[1,2]			Note[A,C]	Note[A,C]	
Ticarcillin-clavulanic acid	Note[1,2]	Note[1,2]			Note[A,C]	Note[A,C]	
Temocillin	-	-			-	-	
Phenoxymethylpenicillin, *S. aureus*	Note[1]	Note[1]			Note[A]	Note[A]	
Phenoxymethylpenicillin, Coagulase-negative staphylococci	-[2]	-[2]			Note[C]	Note[C]	
Oxacillin (screen only), *S. pseudintermedius, S. schleiferi* and *S. coagulans*	NA	NA		1	20[E]	20[E]	

Oxacilline screening: *S. coagulans* toegevoegd

Cephalosporins[1]	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Cefoxitin (screen only), *S. aureus* and coagulase-negative staphylococci except *S. epidermidis* and *S. lugdunensis*	Note[3,4]	Note[3,4]		30	22[A,B]	22[A,B]	
Cefoxitin (screen only), *S. epidermidis* and *S.lugdunensis*	Note[4]	Note[4]		30	27[A,B]	27[A,B]	27
Cefoxitin (screen only), *S. pseudintermedius, S. schleiferi* and *S. coagulans*	Note[5]	Note[5]			Note[C]	Note[C]	

Cefoxitin screening: *S. lugdunensis* toegevoegd aan *S epidermidis*

Erasmus MC Universitair Medisch Centrum Rotterdam Zafung

SWAB Stichting Werkgroep Antibioticabeleid

H+ MC

Neisseria meningitidis

Penicillins[1]	MIC breakpoints (mg/L)		
	S ≤	R >	ATU
Benzylpenicillin (all indications)	0.25	0.25	

All indications

Cefotaxime (all indications)[1]	0.125	0.125	

All indications

Ceftriaxone (all indications including prophylaxis)[1]	0.125	0.125	

All indications including prophylaxis

~~Meropenem (indications other than meningitis)~~	~~Note[2]~~	~~Note[2]~~
Meropenem (all indications)[1,2]	0.25	0.25

All indications: eerder stond er dat je voor ernstige infecties het meningitis breekpunt kon gebruiken

Ciprofloxacin (prophylaxis only)	0.03	0.03	

Prophylaxis only stond eerder als opmerking onder note

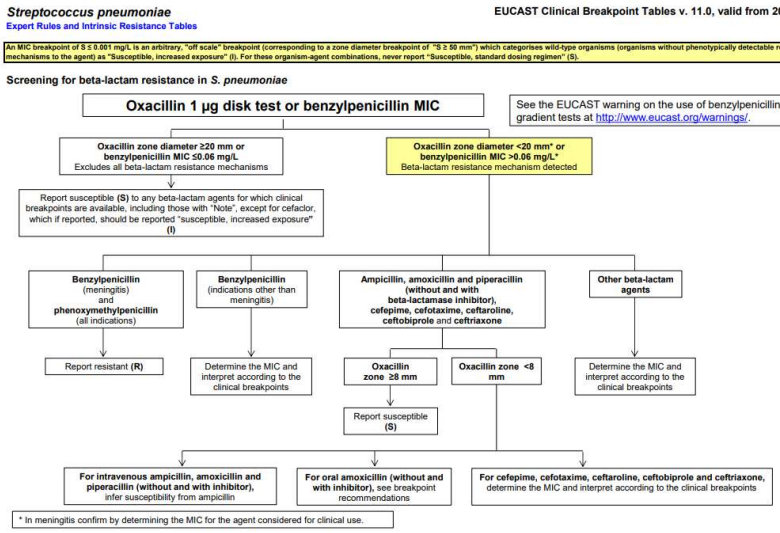
Minocycline (prophylaxis only)	1[1]	1[1]	
Tetracycline (screen only)	2[1]	2[1]	

Idem
Screeningsbreekpunt

Rifampicin (prophylaxis only)	0.25	0.25	

Prophylaxis only stond eerder als opmerking onder note

Oude 2021 schema Pneumokokken



Streptococcus pneumoniae
Expert Rules and Intrinsic Resistance Tables

EUCAST Clinical Breakpoint Tables v. 11.0, valid from 2021-01-01

An MIC breakpoint of S ≤ 0.001 mg/L is an arbitrary, "off scale" breakpoint (corresponding to a zone diameter breakpoint of "S ≥ 50 mm") which categorises wild-type organisms (organisms without phenotypically detectable resistance mechanisms to the agent) as "Susceptible, increased exposure" (I). For these organism-agent combinations, never report "Susceptible, standard dosing regimen" (S).

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 cefaclor, which if reported, should be reported "susceptible, increased exposure" **(I)**

Benzylpenicillin (meningitis) and **phenoxymethylpenicillin** (all indications)

Benzylpenicillin (indications other than meningitis)

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

Other beta-lactam agents

Report resistant **(R)**

Determine the MIC and interpret according to the clinical breakpoints

Oxacillin zone ≥8 mm

Oxacillin zone <8 mm

Report susceptible **(S)**

Determine the MIC and interpret according to the clinical breakpoints

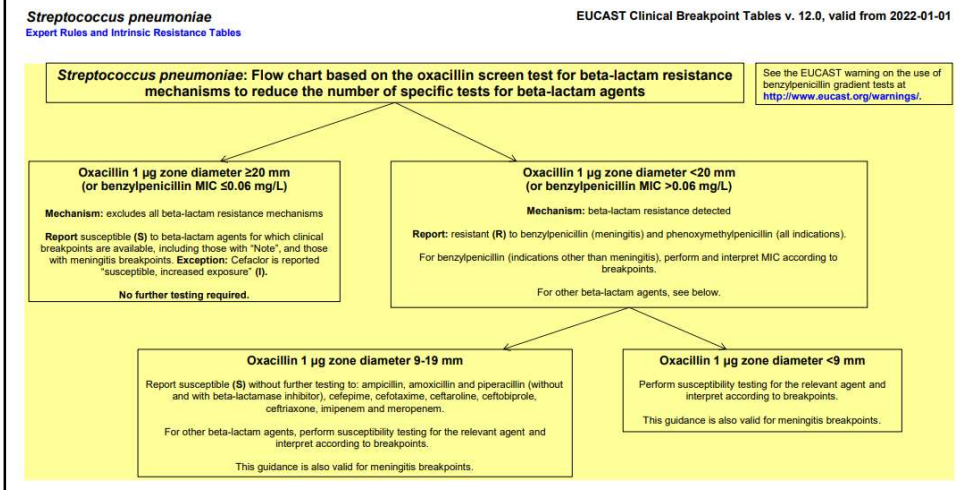
For intravenous ampicillin, amoxicillin and piperacillin (without and with inhibitor), infer susceptibility from ampicillin

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

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

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

Nieuwe schema pneumokokken



Streptococcus pneumoniae
Expert Rules and Intrinsic Resistance Tables

EUCAST Clinical Breakpoint Tables v. 12.0, valid from 2022-01-01

***Streptococcus pneumoniae*: Flow chart based on the oxacillin screen test for beta-lactam resistance mechanisms to reduce the number of specific tests for beta-lactam agents**

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

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", and those with meningitis breakpoints. **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 (meningitis) and phenoxymethylpenicillin (all indications).

For benzylpenicillin (indications other than meningitis), perform and interpret MIC according to breakpoints.

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 other beta-lactam agents, perform susceptibility testing for the relevant agent and interpret according to breakpoints.

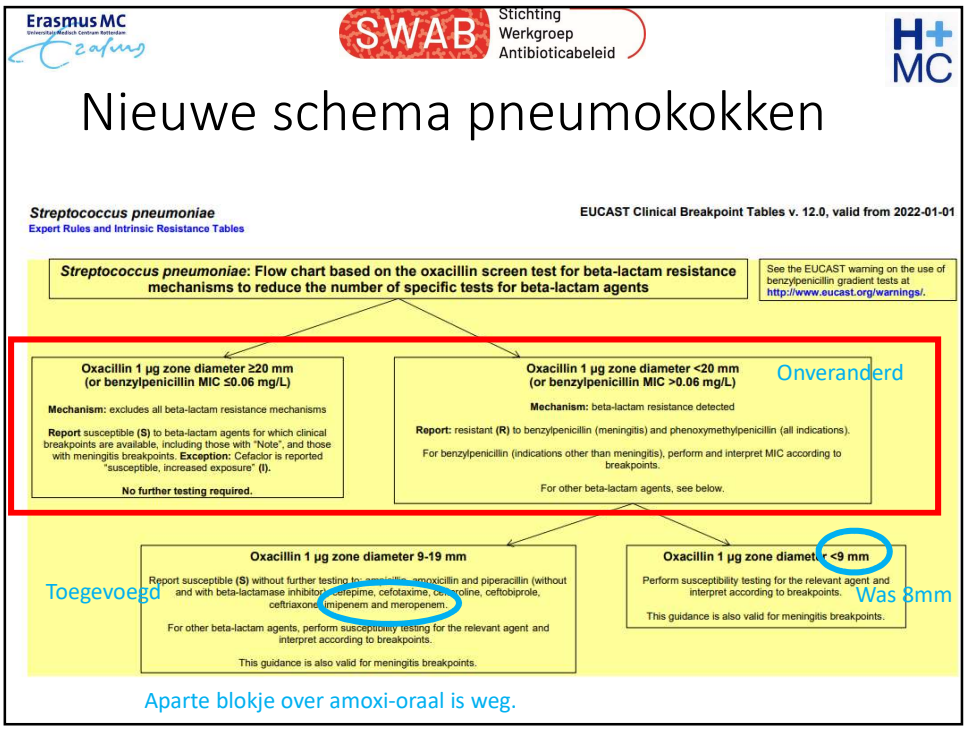
This guidance is also valid for meningitis breakpoints.

Oxacillin 1 µg zone diameter <9 mm

Perform susceptibility testing for the relevant agent and interpret according to breakpoints.

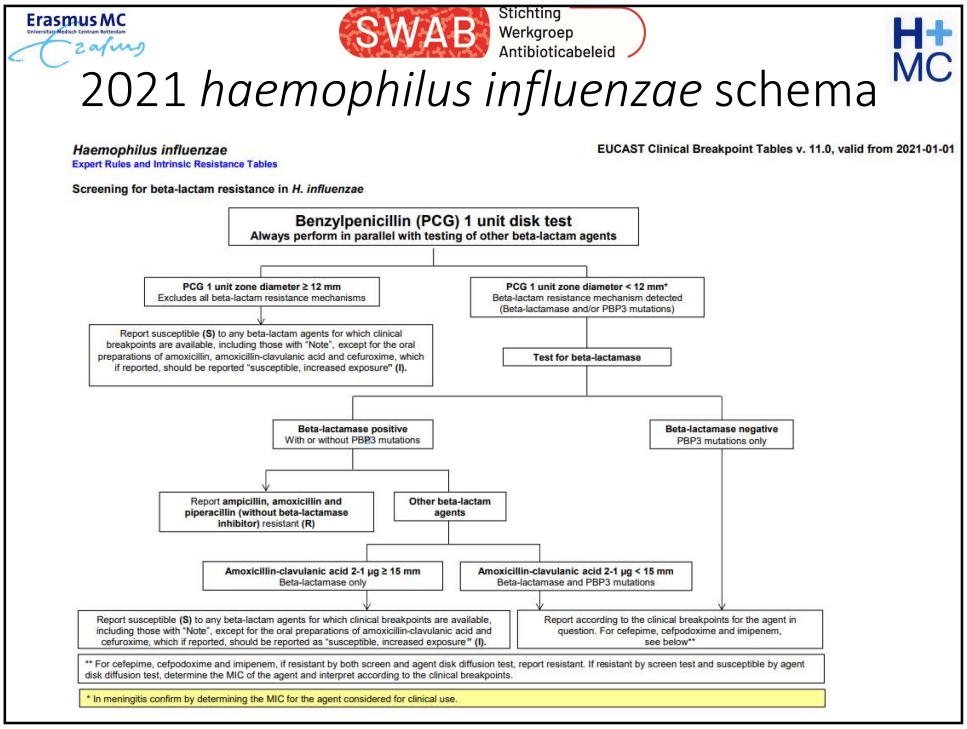
This guidance is also valid for meningitis breakpoints.

Nieuwe schema pneumokokken

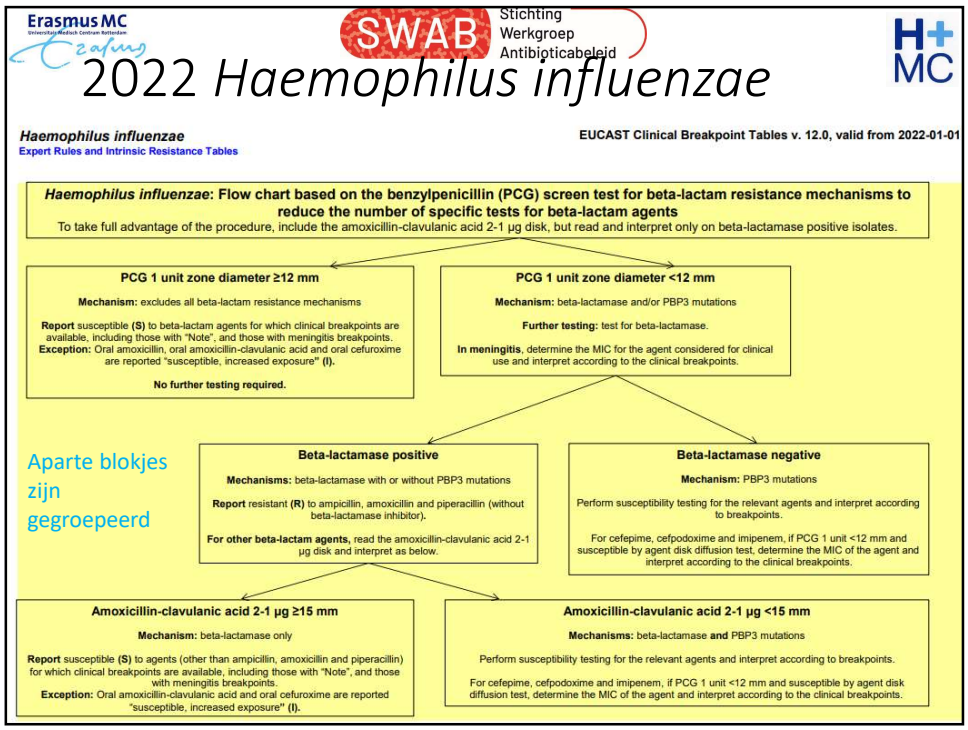


Aparte blokje over amoxi-oraal is weg.

2021 *haemophilus influenzae* schema



2022 *Haemophilus influenzae*



Haemophilus influenzae
Expert Rules and Intrinsic Resistance Tables

EUCAST Clinical Breakpoint Tables v. 12.0, valid from 2022-01-01

***Haemophilus influenzae*: Flow chart based on the benzylpenicillin (PCG) screen test for beta-lactam resistance mechanisms to reduce the number of specific tests for beta-lactam agents**

To take full advantage of the procedure, include the amoxicillin-clavulanic acid 2-1 µg disk, but read and interpret only on beta-lactamase positive isolates.

PCG 1 unit zone diameter ≥12 mm

Mechanism: excludes all beta-lactam resistance mechanisms

Report susceptible **(S)** to beta-lactam agents for which clinical breakpoints are available, including those with "Note", and those with meningitis breakpoints.
Exception: Oral amoxicillin, oral amoxicillin-clavulanic acid and oral cefuroxime are reported "susceptible, increased exposure" **(I)**.

No further testing required.

PCG 1 unit zone diameter <12 mm

Mechanism: beta-lactamase and/or PBP3 mutations

Further testing: test for beta-lactamase.

In meningitis, determine the MIC for the agent considered for clinical use and interpret according to the clinical breakpoints.

Aparte blokjes zijn gegroepeerd

Beta-lactamase positive

Mechanisms: beta-lactamase with or without PBP3 mutations

Report resistant **(R)** to ampicillin, amoxicillin and piperacillin (without beta-lactamase inhibitor).

For other beta-lactam agents, read the amoxicillin-clavulanic acid 2-1 µg disk and interpret as below.

Beta-lactamase negative

Mechanism: PBP3 mutations

Perform susceptibility testing for the relevant agents and interpret according to breakpoints.

For cefepime, cefpodoxime and imipenem, if PCG 1 unit <12 mm and susceptible by agent disk diffusion test, determine the MIC of the agent and interpret according to the clinical breakpoints.

Amoxicillin-clavulanic acid 2-1 µg ≥15 mm

Mechanism: beta-lactamase only

Report susceptible **(S)** to agents (other than ampicillin, amoxicillin and piperacillin) for which clinical breakpoints are available, including those with "Note", and those with meningitis breakpoints.
Exception: Oral amoxicillin-clavulanic acid and oral cefuroxime are reported "susceptible, increased exposure" **(I)**.

Amoxicillin-clavulanic acid 2-1 µg <15 mm

Mechanisms: beta-lactamase **and** PBP3 mutations

Perform susceptibility testing for the relevant agents and interpret according to breakpoints.

For cefepime, cefpodoxime and imipenem, if PCG 1 unit <12 mm and susceptible by agent disk diffusion test, determine the MIC of the agent and interpret according to the clinical breakpoints.

Antifungale middelen

- Opbouw van de tabel is veranderd
- Geen veranderde waarden in de breekpunten
- Aantal andere ECOFF waarden

Nieuwe opbouw van de tabel

Version 3.0, valid from 2022-01-18

Species	Drug	ECOFF (mg/L)	Clinical Breakpoints (mg/L)				Recommendation for area of technical uncertainty (ATU) results
		WT ≤	S ≤	I	R >	ATU	
C. albicans	Amphotericin B	1	1		1		
	Anidulafungin	0.03	0.03		0.03		
	Micafungin	0.016	0.016		0.016	0.03	If S to anidulafungin, report as S and add the following comment: Isolates susceptible to anidulafungin with micafungin MIC of 0.03 mg/L do not harbour an *fks* mutation conferring resistance to the echinocandins. If not S to anidulafungin, report as R and refer to reference laboratory for *fks* sequencing and confirmation of MICs.
	Fluconazole	0.5	2	4	4		
	Itraconazole	0.03	0.06		0.06		
	Posaconazole	0.06	0.06		0.06		
	Voriconazole	0.03	0.06	0.125-0.25	0.25		
	Isavuconazole	ND	ND		ND		
C. dubliniensis	Amphotericin B	0.25	1		1		
	Anidulafungin	ND					
	Micafungin	ND					
	Fluconazole	(0.5)*	2	4	4		
	Itraconazole	0.06	0.06		0.06		
	Posaconazole	0.06	0.06		0.06		
	Voriconazole	0.03	0.06	0.125-0.25	0.25		
	Isavuconazole	ND	ND		ND		
C. glabrata	Amphotericin B	1	1		1		
	Anidulafungin	0.06	0.06		0.06		
	Micafungin	0.03	0.03		0.03		
	Fluconazole	16	0.001	≤16	16		
	Itraconazole	2	ND		ND		
	Posaconazole	1	ND		ND		
	Voriconazole	1	ND		ND		
	Isavuconazole	ND	ND		ND		
C. krusei	Amphotericin B	1	1		1		
	Anidulafungin	0.06	0.06		0.06		
	Micafungin	0.25	ND		ND		
	Fluconazole	128	ND		ND		
	Itraconazole	1	ND		ND		
	Posaconazole	0.5	ND		ND		
	Voriconazole	1	ND		ND		
	Isavuconazole	ND	ND		ND		

Conclusie

- Grootste veranderingen antibacteriële middelen tabel:
  - Aantal antibiotica heeft breekpunten tussen haakjes
  - Aparte screeningsbreekpunten met eigen waarden
  - Nieuwe methode anaerobe disk diffusie
- Kleine aanpassingen in de waarden en in het pneumokokken schema