

Table 6. MIC and zone diameter breakpoints for Enterobacteriaceae (including *Salmonella* and *Shigella* spp.)

The identification of Enterobacteriaceae to species level is essential before applying Expert Rules for the interpretation of susceptibility.

Comments 1-6 relate to urinary tract infections (UTIs) only.

¹UTI recommendations are for organisms associated with uncomplicated urinary infections only. For complicated UTI systemic recommendations should be used.

²If an organism is isolated from multiple sites, for example from blood and urine, interpretation of susceptibility should be made with regard to the systemic site (e.g., if the blood isolate is resistant and the urine isolate susceptible, both should be reported resistant irrespective of the results obtained using interpretative criteria for urine isolates).

³For agents not listed, criteria given for systemic isolates may be used for urinary tract isolates. Intermediate susceptibility infers that the infection may respond as the agent is concentrated at the site of infection.

⁴Direct susceptibility tests on urine samples may be interpreted only if the inoculum gives semi-confluent growth.

⁵In the absence of definitive organism identification, use the recommendations most appropriate for the presumptive identification, accepting that on some occasions the interpretation may be incorrect. A more cautious approach is to use the systemic recommendations.

⁶Coliforms = On-line Medical Dictionary March 2000: "A common name for *E. coli* that is used as an indicator of faecal contamination of water, measured in terms of Coliform count. Occasionally used to refer to all lactose fermenting bacteria."

Table 6. MIC and zone diameter breakpoints for Enterobacteriaceae (including *Salmonella* and *Shigella* spp.)

Antibiotic	MIC breakpoint (mg/L)			Disc content (µg)	Interpretation of zone diameters (mm)			Comment
	R >	I	S ≤		R ≤	I	S ≥	
Aminoglycosides								
Amikacin	16	16	8	30	15	16-18	19	<i>Salmonella</i> spp. should be reported resistant to these agents, irrespective of susceptibility testing result, as they are inactive against <i>Salmonella</i> spp. <i>in vivo</i> . Individual aminoglycoside agents must be tested; susceptibility to other aminoglycosides cannot be inferred from the gentamicin result and <i>vice versa</i> . For streptomycin, the zone diameter breakpoints are valid only for <i>Escherichia coli</i> , <i>Klebsiella</i> spp. and <i>Proteus mirabilis</i> .
Gentamicin	4	4	2	10	16	17-19	20	
Tobramycin	4	4	2	10	17	18-20	21	
Streptomycin	8	-	8	10	12	-	13	

Table 6. MIC and zone diameter breakpoints for Enterobacteriaceae (including *Salmonella* and *Shigella* spp.)

Antibiotic	MIC breakpoint (mg/L)			Disc content (μ g)	Interpretation of zone diameters (mm)			Comment
	R >	I	S \leq		R \leq	I	S \geq	
Penicillins								
Amoxicillin	8	-	8	10	14	-	15	These interpretative standards apply only to <i>Escherichia coli</i> , <i>Salmonella</i> spp. and <i>Proteus mirabilis</i> . They do not apply to species that have chromosomal penicillinases (<i>Klebsiella</i> spp.) or those that typically have inducible AmpC enzymes (e.g. <i>Enterobacter</i> spp., <i>Citrobacter</i> spp. and <i>Serratia</i> spp.).
Ampicillin	8	-	8	10	14	-	15	
Co-amoxiclav	8	-	8	20/10	14	-	15	
Mezlocillin	16	-	16	75	21	-	22	
Mecillinam UTI ¹⁻⁶	8	-	8	10	13	-	14	These interpretative criteria are for <i>E. coli</i> , <i>Klebsiella</i> spp. and <i>P. mirabilis</i> only. Isolates of <i>Escherichia coli</i> and <i>Klebsiella</i> spp. that produce ESBLs often appear susceptible to mecillinam <i>in vitro</i> but clinical efficacy against these organisms is unproven.
Piperacillin	16	-	16	75	23	-	24	
Piperacillin/tazobactam	16	16	8	75/10	20	-	21	The zone diameter breakpoints relate to an MIC of 8 mg/L as no data for the intermediate category are currently available.
Temocillin	8	-	8	30	19	-	20	The distribution of zone diameters for ESBL and AmpC producers straddles the breakpoint. Organisms that appear resistant by disc diffusion should have resistance confirmed by MIC determination.
Temocillin UTI ¹⁻⁶	32	-	32	30	11	-	12	
Ticarcillin/clavulanate	8	-	8	75/10	22	-	23	

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Antibiotic	MIC breakpoint (mg/L)			Disc content (µg)	Interpretation of zone diameters (mm)			Comment
	R >	I	S ≤		R ≤	I	S ≥	
Cephalosporins								
Cefalexin UTI ¹⁻⁶	16	-	16	30	15	-	16	These interpretative criteria are for <i>E. coli</i> and <i>Klebsiella</i> spp. only. Cefalexin results may be used to report susceptibility to cefadroxil. The MIC breakpoint has changed, but a review of the data indicates that no adjustment of the zone diameter breakpoint is necessary.
Cefalexin UTI ¹⁻⁶	16	-	16	30	17	-	18	These interpretative criteria are for <i>P. mirabilis</i> only. Cefalexin results may be used to report susceptibility to cefadroxil.
Cefamandole	8	-	8	30	19	-	20	Zone diameter breakpoints are valid only for <i>Escherichia coli</i> , <i>Klebsiella</i> spp. and <i>Proteus mirabilis</i> . The MIC breakpoints have been adjusted to take account of the MIC distribution for the population lacking a mechanism of resistance.
Cefepime	8	2-8	1	30	26	27-31	32	
Cefixime	1	-	1	5	19	-	20	
Cefoperazone	4	-	4	30	24	-	25	Zone diameter breakpoints are valid only for <i>Escherichia coli</i> , <i>Klebsiella</i> spp. and <i>Proteus mirabilis</i> .
Cefotaxime	2	2	1	30	23	24-29	30	
Cefotetan	4	-	4	30	23	-	24	Zone diameter breakpoints are valid only for <i>Escherichia coli</i> , <i>Klebsiella</i> spp. and <i>Proteus mirabilis</i> .
Cefoxitin	8	-	8	30	19	-	20	The MIC breakpoints have been adjusted to take account of the MIC distribution for the population lacking a mechanism of resistance.
Cefpirome	1	-	1	20	24	-	25	

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Cephalosporins cont.								
Cefpodoxime (ESBL screen)	1	-	1	10	19	-	20	For ESBL detection, all Enterobacteriaceae isolates should be tested with cefpodoxime or both cefotaxime (or ceftriaxone) and ceftazidime. Enterobacteriaceae with resistance to cefpodoxime, ceftriaxone, cefotaxime or ceftazidime should be tested for the presence of ESBLs. Organisms inferred to have ESBLs should be reported resistant to all penicillins (except temocillin) and cephalosporins, including the fourth-generation cephalosporins cefepime and ceftiprome. For serious infections, carbapenems (imipenem, meropenem, doripenem and ertapenem) are the treatment of choice. Organisms with cefpodoxime zone diameters of < 20 mm have a substantive mechanism of resistance. Organisms with zone diameters of 21-25 mm are uncommonly ESBL-producers and may require further investigation.
Ceftazidime	8	2-8	1	30	25	26-29	30	
Ceftibuten	1	-	1	10	27	-	28	
Ceftizoxime	1	-	1	30	29	-	30	
Ceftriaxone	2	2	1	30	23	24-27	28	
Cefuroxime (axetil) UTI¹⁻⁶ only	8	-	8	30	19	-	20	<i>Salmonella</i> spp. should be reported resistant to these agents, irrespective of susceptibility testing result, as they are inactive <i>in-vivo</i> .
Cefuroxime (parenteral)	8	-	8	30	19	-	20	For parenteral cefuroxime the breakpoint pertains to a dosage of 1.5 g three times a day and to <i>E. coli</i> , <i>Klebsiella</i> spp. and <i>P. mirabilis</i> only.

Table 6. MIC and zone diameter breakpoints for Enterobacteriaceae (including <i>Salmonella</i> and <i>Shigella</i> spp.)								
Antibiotic	MIC breakpoint (mg/L)			Disc content (µg)	Interpretation of zone diameters (mm)			Comment
	R >	I	S ≤		R ≤	I	S ≥	
Cephalosporins cont								
Cefalothin	8	-	8	30	26	-	27	The MIC breakpoints have been adjusted to take account of the MIC distribution for the population lacking a mechanism of resistance.
Cefradine	8	-	8	30	11	-	12	
Carbapenems								
Doripenem	4	2-4	1	10	18	19-23	24	Detection of carbapenem resistance is best achieved by use of an MIC method on Mueller Hinton agar. <i>Proteus</i> spp. and <i>Morganella morganii</i> are considered poor targets for imipenem.
Ertapenem	1	1	0.5	10	15	16-27	28	
Imipenem	8	4-8	2	10	16	17-20	21	
Meropenem	8	4-8	2	10	19	20-26	27	
Other β-Lactams								
Aztreonam	8	2-8	1	30	22	23-27	28	The MIC breakpoint has been set to ensure that ESBL-producers with MIC values of 4 mg/L are not interpreted as susceptible to this agent.
Quinolones								
Ciprofloxacin	1	1	0.5	1	16	17-19	20	Isolates of <i>Escherichia coli</i> and <i>Klebsiella</i> spp. with ciprofloxacin MICs of 0.25 and 0.5 mg/L may be reported as resistant. These MICs are higher than those for the 'wild susceptible' populations for the species and may indicate a mechanism of resistance with clinical significance. For ciprofloxacin, there is clinical evidence to indicate a poor response in systemic infections caused by <i>Salmonella</i> spp. with reduced susceptibility to fluoroquinolones (ciprofloxacin MICs 0.125-1 mg/L). It is recommended that the ciprofloxacin MIC should be determined for all invasive salmonellae infection.
Gatifloxacin	1	-	1	2	19	-	20	
Gemifloxacin	0.25	-	0.25	1	19	-	20	
Levofloxacin	2	2	1	1	13	14-16	17	

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Quinolones cont.								
Moxifloxacin	1	1	0.5	1	16	17-19	20	These interpretative criteria are for <i>E. coli</i> , <i>Klebsiella</i> spp., <i>P. mirabilis</i> and coliforms only.
Nalidixic acid UTI ¹⁻⁶	16	-	16	30	17	-	18	
Norfloxacin (Systemic)	1	1	0.5	2	18	19-25	26	
Norfloxacin UTI ¹⁻⁶	4	-	4	2	15	-	16	
Ofloxacin	1	1	0.5	5	25	26-28	29	
Miscellaneous antibiotics								
Azithromycin	-	-	-	-	-	-	-	Azithromycin has been used in the treatment of infections with <i>S. typhi</i> (MIC \leq 16 mg/L for wild type isolates) and some enteric infections.
Chloramphenicol	8	-	8	30	20	-	21	
Colistin	2	-	2	25	19	-	20	Some strains of Enterobacteriaceae (particularly <i>Serratia</i> , <i>Providencia</i> , <i>Citrobacter</i> and <i>Enterobacter</i> spp.) produce clear zones of inhibition with small colonies around the colistin disc. These isolates are resistant as the MICs typically exceed 128 mg/L.
Co-trimoxazole	4	4	2	1.25/ 23.75	15	-	16	The MIC breakpoint is based on the trimethoprim concentration in a 1:19 combination with Sulfamethoxazole. For advice on testing susceptibility to co-trimoxazole, see Appendix 1. The zone diameter breakpoint relates to an MIC of 2 mg/L as no data for the intermediate category are currently available.
Sulfamethoxazole	32	-	32	100	13	-	14	
Trimethoprim UTI ¹⁻⁶	4	4	2	2.5	13	14-16	17	These interpretative criteria are for <i>E. coli</i> , <i>Klebsiella</i> spp., <i>P. mirabilis</i> and coliforms only.

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Miscellaneous antibiotics cont.								
Fosfomycin UTI ¹⁻⁶	32	-	32	200/ 50	24	-	25	These interpretative criteria are for <i>E. coli</i> only. Disc content indicates 200 µg fosfomycin/ 50 µg glucose-6-phosphate.
Fosfomycin UTI ¹⁻⁶	32	-	32	200/ 50	36	-	37	These interpretative criteria are for <i>P. mirabilis</i> only. Disc content indicates 200 µg fosfomycin/ 50 µg glucose-6-phosphate. The susceptibility of <i>Proteus</i> spp. that swarms up to the disc can be difficult to interpret.
Nitrofurantoin UTI	64	-	64	200	16	-	17	These interpretative criteria are for <i>E. coli</i> only.
Tigecycline	2	2	1	15	19	20-23	24	Disc diffusion for Enterobacteriaceae other than <i>E.coli</i> may not give reliable results and for these organisms a gradient test should be used if tigecycline therapy is considered. For <i>E. coli</i> the current disc diffusion breakpoints can be used. Susceptibility of any isolates appearing intermediate or resistant should be confirmed with a gradient test. <i>Morganella morganii</i> , <i>Providencia</i> spp. and <i>Proteus</i> spp. are considered inherently non-susceptible to tigecycline.