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In Vitro Activity of Fosfomycin Against Bacterial Pathogens Isolated from Urine Specimens in Canada from 2007 to 2019: CANWARD Surveillance Study G.G. ZHANEL¹, H.J. ADAM^{1,2}, M.R. BAXTER¹, A. GOLDEN¹, N.M. LAING¹, J.A. KARLOWSKY^{1,2}

Introduction

The current IDSA/ESCMID guidelines recommend a five-seven day course of nitrofurantoin, a three-day course of double-strength trimethoprimsulfamethoxazole (SXT) [in settings where the prevalence of SXT resistance is <10-20%], or a 3g single dose of oral fosfomycin tromethamine as empirical regimens for treating acute uncomplicated bacterial cystitis in otherwise healthy adult nonpregnant females (1). Fluoroquinolones and β -lactams, such as amoxicillin-clavulanate, are second-line therapies (1). High urine concentrations (~4,000 µg/ml, 2-4 hours following a single oral 3g dose) of fosfomycin, potent in-vitro bactericidal activity and high rate of patient compliance due to single dose therapy compared with agents dosed for 3-5 days, likely underlie its reported low rate of resistance development among Escherichia coli (2-4). Currently, CLSI-approved susceptibility breakpoints for fosfomycin exist only for Escherichia coli and Enterococcus faecalis with a MIC ≤64 ug/mI considered susceptible (resistance, ≥256 ug/ml) and it is only approved for testing isolates from urinary tract infections (CLSI M100, 29th Edition (2019). EUCAST also publishes MIC breakpoints for fosfomycin for staphylococci and Enterobacterales with a MIC ≤32 ug/ml considered susceptible (resistance, >32 ug/ml) for both parenteral (systemic infections) and oral (uncomplicated urinary tract infection only) fosfomycin therapy.

Oral fosfomycin, an agent known for >40 years, has received renewed interest recently because of resistance to traditionally used agents (2,4). In addition, IV fosfomycin (which is available in many countries and recently became available in Canada) is indicated for the treatment of a variety of infections including complicated UTI (5,6). However, there is a paucity of published in vitro MIC testing data for fosfomycin because reference MIC testing must use the agar dilution method (4). Recent North American MIC data documenting the activity of fosfomycin against outpatient urinary pathogens other than E. coli and E. faecalis are very limited. Observed and potential increases in antimicrobial resistance among urinary tract pathogens suggest oral and intravenous fosfomycin may be given consideration in the treatment of uncomplicated and complicated urinary tract infections caused by pathogens other than E. coli and E. faecalis.

Materials and Methods

Bacterial isolates

The isolates tested were cultured from urine specimens of outpatients attending emergency departments and submitted to the annual CANWARD surveillance study from 2007 to 2019 (7). Primary isolate identification was performed by the submitting site. If an isolate identification made by the coordinating laboratory (Health Sciences Centre, Winnipeg, Canada) using morphological characteristics and spot tests (7) was not consistent with that provided by the submitting site, the isolate was removed from the study.

Antimicrobial susceptibility testing

Fosfomycin antimicrobial susceptibility testing was performed using CLSI agar dilution testing (MHA supplemented with 25 µg/ml of glucose-6-phosphate; M100 30th edition [2020]); all other antibacterial agents were tested using inhouse-prepared 96-well broth microdilution panels according to CLSI standards (8). Fosfomycin was supplied by Paladin Labs (Montreal, Quebec, Canada). Stock solutions and dilutions were prepared as described by the CLSI (M100 30th edition-2020), in cation-adjusted Mueller-Hinton broth (MHB) (9). Quality control was performed following CLSI recommendations and minimum inhibitory concentrations (MICs) were interpreted using CLSI M100 30th edition [2020] breakpoints and EUCAST criteria (9, 10). Fosfomycin-resistant isolates were each retested to confirm their phenotype. ESBLs were identified following CLSI guidelines (9).

Table 1. In vitro activities of fosfomycin and co isolates collected by 15 laboratories in Canada

Organism (n)	Antimicrobial agent	(µg/ml)			CLSI MIC Interpretation ^a			EUCAST MIC Interpretation ^b			Organism (n) Antin	Antimicrobial ag	ent	(µg/ml)			CLSI MIC Interpretation ^a				EUCAST MIC Interpretation ^b		
		MIC ₅₀	MIC ₉₀	MIC range	% S	% I	% R	% S	% I	% R		Antimicrobial agent		MIC ₅₀	MIC ₉₀	MIC range	% S	% I	% R	% S	% I	% I	
Escherichia coli	Fosfomycin	≤1	4	≤1->512	99.2	0.6	0.2	98.3	-	1.7	Klebsiella	Fosfomycin		16	128	≤1->512	86.1	9.7	4.2	77.8	-	22	
(2785)	SXT⁰	≤0.12	>8	≤0.12->8	75.4	-	24.6	75.4	0.3	24.3	oxytoca	SXT		≤0.12	≤0.12	≤0.12->8	95.8	-	4.2	95.8	0	4.	
	Nitrofurantoin	16	32	≤1->512	97.1	1.8	1.1	98.9	-	1.1	(72)	Nitrofurantoin		32	32	4-256	91.4	5.2	3.4	96.6	-	3.	
	Ciprofloxacin	≤0.06	>16	≤0.06->16	76.3	1.1	22.6	76.3	1.1	22.6		Ciprofloxacin		≤0.06	≤0.06	≤0.06-2	98.6	0	1.4	98.6	0	1.	
	Amoxicillin-clavulanate	4	16	≤0.06->32	82.0	13.2	4.8	98.6	-	1.4		Amoxicillin-clavula	nate	4	16	1->32	88.2	7.4	4.4	98.5	-	1.	
Escherichia coli	Fosfomycin	2	4	≤1->512	96.4	2.1	1.5	96.4	-	3.6	Klebsiella	Fosfomycin		32	256	2-512	86.2	3.5	10.3	79.3		20	
ESBL	SXT	>8	>8	≤0.12->8	35.2	-	64.8	35.2	1.0	63.8	aerogenes	•						0.0			0	20	
(196)	Nitrofurantoin	16	64	≤1-512	88.3	7.6	4.1	95.9	-	4.1	(29)	SXT		≤0.12	0.5	≤0.12-1	100	-	0	100	0		
	Ciprofloxacin	>16	>16	≤0.06->16	14.9	0.9	84.2	14.8	1.0	84.2		Nitrofurantoin		64	128	64-128	0	75.0		75.0		25	
	Amoxicillin-clavulanate	8	32	1->32	51.4	37.7	10.9	96.2	-	3.8		Ciprofloxacin		≤0.06	0.12	≤0.06-8	92.9	0	7.1	92.9	0	7.	
Klebsiella oneumoniae	Fosfomycin	32	128	≤1->512	89.7	4.5	5.8	70.2	-	29.8		Amoxicillin-clavula	nate	>32	>32	2->32	3.7	3.7	92.6	7.4	-	92	
(359)	SXT	≤0.12	>8	≤0.12->8	87.7	-	12.3	87.7	1.4	10.9	Citrobacter freund	ii Fosfomycin		≤1	2	≤1-16	100	0	0	100	-	0	
	Nitrofurantoin	64	128	4->512	36.5	37.1	26.4	73.6	-	26.4	(26)	SXT		≤0.12	>8	≤0.12->8	76.4	-	23.6	76.9	3.9	19.	
	Ciprofloxacin	≤0.06	0.5	≤0.06->16	88.6	3.3	8.1	88.6	3.3	8.1		Nitrofurantoin		16	32	8-32	100	0	0	100	-	0	
	Amoxicillin-clavulanate	2	8	1->32	91.6	5.4	3	99.4	-	0.6		Ciprofloxacin		≤0.06	0.25	≤0.06->16	92.3	3.9	3.8	92.3	3.9	3.	
Klebsiella _.	Fosfomycin	32	256	2->512	78.3	8.7	13	69.6	-	30.4		Amoxicillin-clavula	nate	>32	>32	1->32	8.3	12.5	79.2	33.3	-	66	
oneumoniae ESBL	SXT	>8	>8	≤0.12->8	8.7	_	91.3	8.7	0	91.3	^a CLSI breakpoint	ts for fosfomycin are	onlv ava	ilable for	E. coli (U1	[] only) and <i>L</i>	E. faeca	lis (UT	l onlv):	MIC ≤6₄	4 ua/mi	.l =	
(23)	Nitrofurantoin	>0 64	-0 512	32-512	26.3	36.9	36.8	63.2	U	36.8	susceptible, MIC	128 ug/ml = interme	diate, an										
(23)	Ciprofloxacin	4	>16	≤0.06->16	26.1	4.3	69.6	26.1	4.3	69.6		gens in CLSI colum points for fosfomycir		robactera	les (uncor	nplicated UT	l only) a	and Sta	aphyloc	occus			
	Amoxicillin-clavulanate	16	32	4->32	28.6	42.8	28.6	95.2	ч.0 -	4.8	(intravenous): MI	C ≤32 ug/ml = susce	ptible an		•	•	• •				kpoints	s fo	
		10	02	1 2 0 2	20.0	12.0	20.0	00.2			Enterococcus of	Pseudomonas aerug	jinosa.										
Enterococcus	Fostomycin	64	100	1 > 512	00 2	10.2	15	ΝΛ	NΙΛ	ΝΛ	^c UD, Unable to d	letermine.											
faecalis	Fosfomycin	64	128	4->512	88.3	10.2	1.5	NA	NA	NA	^d % Susceptible i	ncluded isolates cate				creased expo	sure'.						
faecalis	SXT	≤0.12	0.5	≤0.12->8	NA	NA	NA	UDc	NA UD	UD	^d % Susceptible in ^e AMC activity pre ^f AMC activity pre	ncluded isolates cate edicted by testing an edicted by testing cel	picillin fo	r <i>E. faeca</i> S. aureus	alis. 5.	-							
faecalis	SXT Nitrofurantoin		0.5 16	≤0.12->8 2-128	NA 99.6	NA 0	NA 0.4	UD ^c 99.6		UD 0.4	^d % Susceptible in ^e AMC activity pre ^f AMC activity pre SXT, trimethoprin	ncluded isolates cate edicted by testing an	picillin fo	r <i>E. faeca</i> S. aureus	alis. 5.	-		xicillin-	clavula	nate; N	A, not		
faecalis	SXT Nitrofurantoin Ciprofloxacin	≤0.12 8 1	0.5	≤0.12->8 2-128 0.12->16	NA 99.6 67.1	NA	NA	UD ^c 99.6 76.7	UD - -	UD 0.4 23.3	^d % Susceptible in ^e AMC activity pre ^f AMC activity pre	ncluded isolates cate edicted by testing an edicted by testing cel	picillin fo	r <i>E. faeca</i> S. aureus	alis. 5.	-		xicillin-	clavula	nate; N	A, not		
faecalis (333)	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate	≤0.12	0.5 16 >16 1	≤0.12->8 2-128 0.12->16 0.12-2	NA 99.6 67.1 100 ^e	NA 0 9.0 -	NA 0.4 23.9 0	UD ^c 99.6 76.7 100		UD 0.4 23.3 0	^d % Susceptible in ^e AMC activity pre ^f AMC activity pre SXT, trimethoprin	ncluded isolates cate edicted by testing an edicted by testing cel	picillin fo	r <i>E. faeca</i> S. aureus	alis. 5.	-		xicillin-	clavula	nate; N	A, not		
faecalis (333) Proteus mirabilis	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate	≤0.12 8 1 0.5 4	0.5 16 >16 1 128	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512	NA 99.6 67.1 100 ^e 86.9	NA 0	NA 0.4 23.9 0 4.8	UD ^c 99.6 76.7 100 81.4	UD - - 0 -	UD 0.4 23.3 0 18.6	^d % Susceptible in ^e AMC activity pre ^f AMC activity pre SXT, trimethoprin applicable.	ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole;	picillin fo oxitin for NIT, nitro	r <i>E. faeca</i> <i>S. aureus</i> furantoin;	alis. s. CIP, cipr	ofloxacin; AM	IC, amc						
faecalis (333) Proteus mirabilis	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT	≤0.12 8 1 0.5 4 ≤0.12	0.5 16 >16 1 128 >8	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8	NA 99.6 67.1 100 ^e 86.9 77.2	NA 0 9.0 - 8.3 -	NA 0.4 23.9 0 4.8 22.8	UD ^c 99.6 76.7 100 81.4 77.2	UD - -	UD 0.4 23.3 0 18.6 22.1	^d % Susceptible in ^e AMC activity pre ^f AMC activity pre SXT, trimethoprin applicable.	ncluded isolates cate edicted by testing an edicted by testing cel	picillin fo oxitin for NIT, nitro	r <i>E. faeca</i> <i>S. aureus</i> furantoin;	alis. s. CIP, cipr	ofloxacin; AM	IC, amc						
Enterococcus faecalis (333) Proteus mirabilis (145)	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin	≤0.12 8 1 0.5 4 ≤0.12 128	0.5 16 >16 1 128	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8 64-512	NA 99.6 67.1 100 ^e 86.9 77.2 0	NA 0 9.0 - 8.3 - 16.9	NA 0.4 23.9 0 4.8 22.8 83.1	UD ^c 99.6 76.7 100 81.4 77.2 16.9	UD - 0 - 0.7 -	UD 0.4 23.3 0 18.6 22.1 83.1	^d % Susceptible in ^e AMC activity pre ^f AMC activity pre SXT, trimethoprin applicable. Table 2. MIC dis	ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole;	picillin fo oxitin for NIT, nitro	r <i>E. faeca</i> <i>S. aureus</i> furantoin;	alis. S. CIP, cipr Irine isol	ofloxacin; AM	IC, amc	15 lab					
faecalis (333) Proteus mirabilis	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin	≤0.12 8 1 0.5 4 ≤0.12	0.5 16 >16 1 128 >8 128 4	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8 64-512 ≤0.06->16	NA 99.6 67.1 100 ^e 86.9 77.2 0 83.4	NA 0 9.0 - 8.3 - 16.9 0.7	NA 0.4 23.9 0 4.8 22.8 83.1 15.9	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4	UD - - 0 -	UD 0.4 23.3 0 18.6 22.1 83.1 15.9	^d % Susceptible in ^e AMC activity pre ^f AMC activity pre SXT, trimethoprin applicable. Table 2. MIC dis 2007 to 2019.	ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole;	picillin fo oxitin for NIT, nitro	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u	alis. S. CIP, cipr urine isol	ofloxacin; AM ates collect	IC, amc ed by ⁻ <mark>C (µg/m</mark>	15 labo	oratori				
faecalis 333) Proteus mirabilis 145)	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate	≤0.12 8 1 0.5 4 ≤0.12 128	0.5 16 >16 1 128 >8	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8 64-512	NA 99.6 67.1 100 ^e 86.9 77.2 0	NA 0 9.0 - 8.3 - 16.9	NA 0.4 23.9 0 4.8 22.8 83.1	UD ^c 99.6 76.7 100 81.4 77.2 16.9	UD - 0 - 0.7 -	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8	^d % Susceptible in ^e AMC activity pre ^f AMC activity pre SXT, trimethoprin applicable. Table 2. MIC dis	ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole;	picillin fo oxitin for NIT, nitro	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u	alis. S. CIP, cipr urine isol	ofloxacin; AM lates collect osfomycin M /e % of isolat	IC, amc ed by ⁻ <mark>C (µg/m</mark>	15 labo	oratori		anada	ı fra	
aecalis 333) Proteus mirabilis 145) Pseudomonas	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin	≤0.12 8 1 0.5 4 ≤0.12 128	0.5 16 >16 1 128 >8 128 4	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8 64-512 ≤0.06->16	NA 99.6 67.1 100 ^e 86.9 77.2 0 83.4	NA 0 9.0 - 8.3 - 16.9 0.7	NA 0.4 23.9 0 4.8 22.8 83.1 15.9	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4	UD - 0 - 0.7 -	UD 0.4 23.3 0 18.6 22.1 83.1 15.9	^d % Susceptible in ^e AMC activity pre ^f AMC activity pre SXT, trimethoprin applicable. Table 2. MIC dis 2007 to 2019.	ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole; stributions for fost	omycin	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u	alis. S. CIP, cipr urine isol	ofloxacin; AM ates collect osfomycin M /e % of isolat 16	IC, amc ed by ⁻ C (µg/m es inhib	15 labo I) ^a ited at	oratori MIC	es in C	anada	1 frc	
aecalis 333) Proteus mirabilis 145) Pseudomonas aeruginosa	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate	≤0.12 8 1 0.5 4 ≤0.12 128 ≤0.06 1	0.5 16 >16 1 128 >8 128 4 8	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8 64-512 ≤0.06->16 0.5->32	NA 99.6 67.1 100 ^e 86.9 77.2 0 83.4 93.0	NA 0 9.0 - 8.3 - 16.9 0.7 2.8	NA 0.4 23.9 0 4.8 22.8 83.1 15.9 4.2	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4 97.2	UD - 0 - 0.7 - 0.7 - 0.7 -	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8	^d % Susceptible in ^e AMC activity pre ^f AMC activity pre SXT, trimethoprin applicable. Table 2. MIC dis 2007 to 2019. Genus/species (n	ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole; stributions for fost	omycin omycin 2 88.0	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u	alis. S. CIP, cipr Irine isol	ofloxacin; AM ates collect osfomycin M /e % of isolat 16 3 97.2 9	IC, amc ed by ⁻ C (µg/m es inhib	15 labo I) ^a ited at 64	oratori MIC 128	es in C	anada 6 9	511 100	
aecalis 333) Proteus mirabilis 145) Pseudomonas aeruginosa	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin	≤0.12 8 1 0.5 4 ≤0.12 128 ≤0.06 1	0.5 16 >16 1 128 >8 128 4 8 256	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8 64-512 ≤0.06->16 0.5->32 ≤1->512	NA 99.6 67.1 100 ^e 86.9 77.2 0 83.4 93.0 49.2	NA 0 9.0 - 8.3 - 16.9 0.7 2.8 37.1	NA 0.4 23.9 0 4.8 22.8 83.1 15.9 4.2 13.7	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4 97.2 NA	UD - 0 - 0.7 - 0.7 - 0.7 - NA	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8 NA	 ^d % Susceptible in ^e AMC activity presson ^f AMC activity presson ^g SXT, trimethoprinal applicable. Table 2. MIC disson 2007 to 2019. Genus/species (no Escherichia coli (ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole; stributions for fost (2785) 59.5 ESBL (196) 49.5	omycin omycin 2 88.0 87.8	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u 4 94.2 93.9	alis. CIP, cipr urine isol Cumulativ 8 95.7 94.9	ofloxacin; AM ates collect osfomycin M <u>/e % of isolat</u> 16 97.2 95.9 9	IC, amc ed by C (µg/m es inhib i2 3.3 5.4	15 lab ited at 64 99.2	oratori MIC 128 99.8 98.5	es in C 250 99. 99.	anada 6 9 0	511 511 100	
aecalis 333) Proteus mirabilis 145) Pseudomonas aeruginosa	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT	≤0.12 8 1 0.5 4 ≤0.12 128 ≤0.06 1 128 8	0.5 16 >16 1 128 >8 128 4 8 256 >8	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8 64-512 ≤0.06->16 0.5->32 ≤1->512 1->8	NA 99.6 67.1 100° 86.9 77.2 0 83.4 93.0 49.2 NA	NA 0 9.0 - 8.3 - 16.9 0.7 2.8 37.1 NA	NA 0.4 23.9 0 4.8 22.8 83.1 15.9 4.2 13.7 NA	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4 97.2 NA NA	UD - 0 - 0.7 - 0.7 - NA NA	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8 NA NA	 ^d % Susceptible in ^e AMC activity pre ^f AMC activity pre SXT, trimethoprin applicable. Table 2. MIC dis 2007 to 2019. Genus/species (n Escherichia coli (Escherichia coli (Klebsiella pneum) 	ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole; stributions for fost (2785) 59.5 ESBL (196) 49.5 noniae (359) 0.3	omycin omycin 2 88.0 87.8 1.9	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u 4 94.2	alis. CIP, cipr Irine isol Cumulativ 8 95.7 94.9 10.9	ofloxacin; AM ates collect osfomycin M /e % of isolat 16 97.2 95.9 9 34.8 7	IC, amc ed by С (µg/m es inhib 2 3.3 5.4 5.4	15 lab ited at 64 99.2 89.7	oratori <u>MIC</u> 128 99.8 98.5 94.2	es in C 250 99. 99. 96.	anada 6 9 0 9	512 512 100 100	
faecalis (333) Proteus mirabilis	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin	≤0.12 8 1 0.5 4 ≤0.12 128 ≤0.06 1 128 8 ×512	0.5 16 >16 1 128 >8 128 4 8 256 >8	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8 64-512 ≤0.06->16 0.5->32 ≤1->512 1->8 512->512	NA 99.6 67.1 100° 86.9 77.2 0 83.4 93.0 49.2 NA NA	NA 0 9.0 - 8.3 - 16.9 0.7 2.8 37.1 NA NA	NA 0.4 23.9 0 4.8 22.8 83.1 15.9 4.2 13.7 NA NA	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4 97.2 NA NA NA	UD - 0 - 0.7 - 0.7 - NA NA	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8 NA NA NA	 ^d % Susceptible in ^e AMC activity presson ^f AMC activity presson ^g SXT, trimethoprinal applicable. Table 2. MIC disson 2007 to 2019. Genus/species (no Escherichia coli (ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole; stributions for fost (2785) 59.5 ESBL (196) 49.5 noniae (359) 0.3	omycin omycin 2 88.0 87.8	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u 4 94.2 93.9	alis. CIP, cipr urine isol Cumulativ 8 95.7 94.9	ofloxacin; AM ates collect osfomycin M /e % of isolat 16 97.2 95.9 9 34.8 7	IC, amc ed by С (µg/m es inhib 2 3.3 5.4 5.4	15 lab ited at 64 99.2	oratori MIC 128 99.8 98.5	es in C 250 99. 99. 96.	anada 6 9 0 9	512 512 100 100	
aecalis 333) Proteus mirabilis 145) Pseudomonas aeruginosa 124) Staphylococcus	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate	≤0.12 8 1 0.5 4 ≤0.12 128 ≤0.06 1 128 8 >512 0.25	0.5 16 >16 1 128 >8 128 4 8 256 >8 >512 8	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8 64-512 ≤0.06->16 0.5->32 ≤1->512 1->8 512->512 ≤0.06->16	NA 99.6 67.1 100 ^e 86.9 77.2 0 83.4 93.0 49.2 NA NA NA 75.8	NA 0 9.0 - 8.3 - 16.9 0.7 2.8 37.1 NA NA 5.7	NA 0.4 23.9 0 4.8 22.8 83.1 15.9 4.2 13.7 NA NA NA 18.5	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4 97.2 NA NA NA NA NA	UD - 0 - 0.7 - 0.7 - NA NA NA NA NA -	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8 NA NA NA NA NA 24.2	 ^d % Susceptible in ^e AMC activity present ^f AMC activity present ^f AMC activity present ^g AMC activity present SXT, trimethopring applicable. Table 2. MIC dissent 2007 to 2019. Genus/species (no Escherichia coli (Escherichia coli - Klebsiella pneum Klebsiella pneum 	ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole; stributions for fost (2785) 59.5 ESBL (196) 49.5 noniae (359) 0.3 noniae-ESBL	omycin omycin 2 88.0 87.8 1.9	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u 4 94.2 93.9	alis. CIP, cipr Irine isol Cumulativ 8 95.7 94.9 10.9	ofloxacin; AM ates collect osfomycin M /e % of isolat 16 97.2 95.9 95.9 95.9 95.9 95.9 95.9 95.9 95	IC, amc ed by C (μg/m es inhib 3.3 5.4 0.2 9.6	15 lab ited at 64 99.2 89.7	oratori <u>MIC</u> 128 99.8 98.5 94.2	es in C 250 99. 99. 96. 95.	anada 6 9 0 9 7	51 2 100 100 100	
aecalis 333) Proteus mirabilis 145) Pseudomonas aeruginosa 124) Staphylococcus aureus	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin	≤0.12 8 1 0.5 4 ≤0.12 128 ≤0.06 1 128 8 >512 0.25 >32 8	0.5 16 >16 1 128 >8 128 4 8 256 >8 >512 8 >512 8 >512 8 >32	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8 64-512 ≤0.06->16 0.5->32 ≤1->512 1->8 512->512 ≤0.06->16 32->32 ≤1-256	NA 99.6 67.1 100 ^e 86.9 77.2 0 83.4 93.0 49.2 NA NA 75.8 NA 98.9	NA 0 9.0 - 8.3 - 16.9 0.7 2.8 37.1 NA NA 5.7 NA	NA 0.4 23.9 0 4.8 22.8 83.1 15.9 4.2 13.7 NA NA NA 18.5	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4 97.2 NA NA NA 75.8 ^d NA 97.8	UD - 0 0.7 - 0.7 - 0.7 - NA NA NA NA NA NA NA - NA	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8 NA NA NA 24.2 NA 24.2 NA 2.2	 ^d % Susceptible in ^e AMC activity present ^f AMC activity present ^f AMC activity present ^g AMC activity present ^f AMC a	ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole; stributions for fost (2785) 59.5 ESBL (196) 49.5 noniae (359) 0.3 noniae-ESBL ecalis (333)	omycin omycin 2 88.0 87.8 1.9	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u 94.2 93.9 4.5	alis. CIP, cipr Irine isol Cumulativ 8 95.7 94.9 10.9 8.7	ofloxacin; AM ates collect osfomycin M /e % of isolat 16 3 97.2 94 95.9 94 34.8 74 43.5 65 1.8 34	IC, amc ed by C (µg/m es inhib 2 3.3 5.4 0.2 9.6 4.2	15 lab ited at 64 99.2 89.7 78.3	oratori MIC 128 99.8 98.5 94.2 87.0	es in C 250 99. 99. 96. 95.	anada 6 9 0 9 7 4	512 100 100 100 100	
aecalis 333) Proteus mirabilis 145) Pseudomonas aeruginosa 124) Staphylococcus	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate	≤0.12 8 1 0.5 4 ≤0.12 128 ≤0.06 1 128 8 >512 0.25 >32 8 ≤0.12	0.5 16 >16 1 28 28 128 4 8 256 >8 >512 8 >512 8 >512 8 >32 32 32	≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.12->8 64-512 ≤0.06->16 0.5->32 ≤1->512 ≤1->512 ≤0.06->16 32->32 ≤1-256 ≤0.12-0.5	NA 99.6 67.1 100° 86.9 77.2 0 83.4 93.0 49.2 NA 49.2 NA 75.8 NA 98.9 100	NA 0 9.0 - 8.3 - 16.9 0.7 2.8 37.1 NA NA 5.7 NA	NA 0.4 23.9 0 4.8 22.8 83.1 15.9 4.2 13.7 NA NA NA 18.5	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4 97.2 NA NA NA 75.8 ^d NA 97.8 100	UD - 0 - 0.7 - 0.7 - NA NA NA NA NA -	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8 NA NA NA 24.2 NA 24.2 NA 2.2 0	 ^d % Susceptible in ^e AMC activity present ^f AMC a	ncluded isolates cate edicted by testing an edicted by testing cell n-sulfamethoxazole; stributions for fost (2785) ≤ 11 (2785) ≤ 59.5 ESBL (196) 49.5 noniae (359) 0.3 noniae -ESBL ecalis (333) $\leq (145)$ 9.0	omycin omycin 2 88.0 87.8 1.9 4.3	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u 94.2 93.9 4.5 0.3	alis. CIP, cipr Irine isol Cumulativ 8 95.7 94.9 10.9 8.7 0.6	ofloxacin; AM ates collect osfomycin M /e % of isolat 16 37.2 95.9 95.9 95.9 95.9 95.9 95.9 95.9 95	IC, amc ed by C (μg/m es inhib 3.3 5.4 5.4 5.4 5.4 5.4 5.4 5.4 5.4 5.4 5.4	15 lab ited at 64 99.2 89.7 78.3 88.3	oratori MIC 128 99.8 98.5 94.2 87.0 98.5	es in C 250 99. 99. 96. 95. 99. 96.	anada 6 9 0 9 7 4 6	51 2 100 100 100 100 100	
aecalis 333) Proteus mirabilis 145) Pseudomonas aeruginosa 124) Staphylococcus	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate	≤0.12 8 1 0.5 4 ≤0.12 128 ≤0.06 1 128 8 >512 0.25 >32 8 ≤0.12 16	0.5 16 >16 1 128 >8 128 4 8 256 >8 >512 8 >512 8 >512 8 >32 32 32 32 16	$\leq 0.12 -> 8$ 2-128 0.12->16 0.12-2 $\leq 1->512$ $\leq 0.12-> 8$ 64-512 $\leq 0.06->16$ 0.5->32 $\leq 1->512$ $\leq 1->512$ $\leq 0.06->16$ 32->32 $\leq 1-256$ $\leq 0.12-0.5$ 4-32	NA 99.6 67.1 100° 86.9 77.2 0 83.4 93.0 49.2 NA 49.2 NA 75.8 NA 98.9 100 100	NA 0 9.0 - 8.3 - 16.9 0.7 2.8 37.1 NA 37.1 NA 5.7 NA 0 - 0	NA 0.4 23.9 0 4.8 22.8 83.1 15.9 4.2 13.7 NA 18.5 NA 18.5 NA 1.1 0 0	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4 97.2 NA NA NA 75.8 ^d NA 97.8 100 NA	UD - 0 - 0.7 - 0.7 - 0.7 - NA NA NA NA NA NA NA O	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8 NA NA 2.8 NA 2.2 NA 2.2 0 NA	 ^d % Susceptible in ^e AMC activity prest AMC activity prest AMC activity prest AMC activity prest SXT, trimethoprimapplicable. Table 2. MIC dist 2007 to 2019. Genus/species (n Escherichia coli (Escherichia coli (Escherichia coli (Escherichia coli (Klebsiella pneum Klebsiella pneum (23) Enterococcus fae Proteus mirabilis Pseudomonas ae (124) 	ncluded isolates cate edicted by testing an edicted by testing cell n-sulfamethoxazole; stributions for fost (2785) ≤ 11 (2785) ≤ 59.5 ESBL (196) 49.5 noniae (359) 0.3 noniae-ESBL ecalis (333) $\leq (145) \qquad 9.0$ eruginosa $\qquad 0.8$	omycin omycin 0 2 88.0 87.8 1.9 4.3 30.3	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u 94.2 93.9 4.5 0.3 60.0 4.8	alis. CIP, cipr Irine isol Cumulativ 8 95.7 94.9 10.9 8.7 0.6 69.7	ofloxacin; AM ates collect osfomycin M <u>/e % of isolat</u> 16 97.2 95.9 95.9 95.9 94.8 70 43.5 61 1.8 34.8 75.2 8 10.5	IC, amc ed by C (µg/m es inhib 2 3.3 5.4 0.2 9.6 4.2 1.4 5.9	15 lab ited at 64 99.2 89.7 78.3 88.3 88.3 86.9 49.2	oratori MIC 128 99.8 98.5 94.2 87.0 98.5 95.2	es in C 250 99. 99. 96. 95. 95.	anada 6 9 0 9 7 4 6 2	51 2 100 100 100 100 100	
aecalis 333) Proteus mirabilis 145) Pseudomonas aeruginosa 124) Staphylococcus aureus	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate	≤0.12 8 1 0.5 4 ≤0.12 128 ≤0.06 1 128 8 >512 0.25 >32 8 ≤0.12 16 0.5	0.5 16 >16 1 128 >8 128 4 8 256 >8 >512 8 >512 8 >512 8 >32 32 32 ≤0.12 16 >16	$\leq 0.12 -> 8$ 2-128 0.12->16 0.12-2 $\leq 1->512$ $\leq 0.12-> 8$ 64-512 $\leq 0.06->16$ 0.5->32 $\leq 1->512$ 1-> 8 512->512 $\leq 0.06->16$ 32->32 $\leq 1-256$ $\leq 0.12-0.5$ 4-32 0.12->16	NA 99.6 67.1 100° 86.9 77.2 0 83.4 93.0 49.2 NA 49.2 NA 75.8 NA 98.9 100 100 55.7	NA 0 9.0 - 8.3 - 16.9 0.7 2.8 37.1 NA 5.7 NA 5.7 NA 0 -	NA 0.4 23.9 0 4.8 22.8 83.1 15.9 4.2 13.7 NA 18.5 NA 18.5 NA 1.1 0 0 43.2	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4 97.2 NA 97.2 NA NA 75.8 ^d NA 97.8 100 NA 97.8	UD - 0 0.7 - 0.7 - 0.7 - NA NA NA NA - NA - 0 NA - 0 NA -	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8 NA NA 24.2 NA 24.2 NA 2.2 0 NA 44.3	 ^d % Susceptible in ^e AMC activity prest SXT, trimethoprima applicable. Table 2. MIC dist 2007 to 2019. Genus/species (n Escherichia coli (Escherichi	ncluded isolates cate edicted by testing an edicted by testing cel n-sulfamethoxazole; stributions for fost (2785) ≤ 10 (2785) ≤ 59.5 ESBL (196) 49.5 noniae (359) 0.3 noniae (359) 0.3 noniae-ESBL ecalis (333) $\leq (145)$ 9.0 eruginosa 0.8 aureus (89) 6.7	omycin omycin 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u 94.2 93.9 4.5 0.3 60.0 4.8 47.2	Alis. CIP, cipr Irine isol Cumulativ 8 95.7 94.9 10.9 8.7 0.6 69.7 73.0	ofloxacin; AM ates collect osfomycin M <u>/e % of isolat</u> 16 97.2 95.9 95.9 95.9 95.9 95.9 34.8 7 43.5 6 1.8 3 75.2 8 10.5 10.5	IC, amc ed by C (µg/m es inhib 3.3 5.4 0.2 9.6 4.2 1.4 5.9 7.8	15 lab ited at 64 99.2 89.7 78.3 88.3 86.9 49.2 98.9	oratori MIC 128 99.8 98.5 94.2 87.0 98.5 95.2 86.3	es in C 250 99. 99. 96. 95. 99. 96. 95.	anada 6 9 0 9 7 4 6 2 0	51 2 100 100 100 100 100	
aecalis 333) Proteus mirabilis 145) Pseudomonas aeruginosa 124)	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate	≤0.12 8 1 0.5 4 ≤0.12 128 ≤0.06 1 128 8 >512 0.25 >32 8 ≤0.12 16 0.5 4	0.5 16 >16 1 28 28 128 4 8 256 >8 >512 8 >512 8 >512 8 >32 32 32 ≤0.12 16 >16 >16 >32	 ≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.06->16 0.5->32 ≤1->512 1->8 512->512 ≤0.06->16 32->32 ≤1-256 ≤0.12-0.5 4-32 0.12->16 0.5->32 	NA 99.6 67.1 100° 86.9 77.2 0 83.4 93.0 49.2 NA 49.2 NA 75.8 NA 98.9 100 100 55.7 73.3 ^f	NA 0 9.0 - 8.3 - 16.9 0.7 2.8 37.1 NA 5.7 NA 5.7 NA 0 - 0 1.1 -	NA 0.4 23.9 0 4.8 22.8 83.1 15.9 4.2 13.7 NA 18.5 NA 1.1 0 0 43.2 26.7	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4 97.2 NA 97.2 NA 75.8 ^d NA 97.8 100 NA 97.8 100 NA 55.7 ^d NA	UD - 0 - 0.7 - 0.7 - 0.7 - NA NA NA NA NA NA NA O	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8 NA NA 2.2 NA 2.2 0 NA 2.2 0 NA 44.3 NA	 ^d % Susceptible in ^e AMC activity pressure f AMC activity activity pressure f AMC activity acti	ncluded isolates cate edicted by testing an edicted by testing celladicted by testing celln-sulfamethoxazole;atributions for fostatributions fost <td>omycin omycin 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0</br></br></td> <td>r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u 94.2 93.9 4.5 0.3 60.0 4.8</td> <td>Alis. CIP, cipr Irine isol Cumulativ 8 95.7 94.9 10.9 8.7 0.6 69.7 73.0 27.8</td> <td>ofloxacin; AM ates collect osfomycin M /e % of isolat 16 97.2 95.9 95.9 95.9 95.9 95.9 95.9 95.9 95</td> <td>IC, amc ed by C (µg/m es inhib 2 3.3 5.4 0.2 9.6 4.2 1.4 5.9 7.8 7.0</td> <td>15 lab ited at 64 99.2 89.7 78.3 88.3 86.9 49.2 98.9 67.1</td> <td>oratori MIC 128 99.8 98.5 94.2 87.0 98.5 95.2 86.3 79.7</td> <td>es in C 250 99. 99. 96. 95. 99. 96. 95. 100 86.</td> <td>anada 6 9 0 9 7 4 6 2 2 0 1</td> <td>512 100 100 100 100 100</td>	omycin omycin 0 0 0 	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u 94.2 93.9 4.5 0.3 60.0 4.8	Alis. CIP, cipr Irine isol Cumulativ 8 95.7 94.9 10.9 8.7 0.6 69.7 73.0 27.8	ofloxacin; AM ates collect osfomycin M /e % of isolat 16 97.2 95.9 95.9 95.9 95.9 95.9 95.9 95.9 95	IC, amc ed by C (µg/m es inhib 2 3.3 5.4 0.2 9.6 4.2 1.4 5.9 7.8 7.0	15 lab ited at 64 99.2 89.7 78.3 88.3 86.9 49.2 98.9 67.1	oratori MIC 128 99.8 98.5 94.2 87.0 98.5 95.2 86.3 79.7	es in C 250 99. 99. 96. 95. 99. 96. 95. 100 86.	anada 6 9 0 9 7 4 6 2 2 0 1	512 100 100 100 100 100	
aecalis 333) Proteus mirabilis 145) Pseudomonas teruginosa 124) Staphylococcus tureus 89)	SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin SXT Nitrofurantoin Ciprofloxacin Amoxicillin-clavulanate Fosfomycin	 ≤0.12 8 1 0.5 4 ≤0.12 128 ≤0.06 1 128 8 >512 0.25 >32 8 ≤0.12 16 0.5 4 32 	0.5 16 >16 1 128 >8 128 4 8 256 >8 >512 8 >512 8 >512 8 >32 32 32 ≤0.12 16 >16	 ≤0.12->8 2-128 0.12->16 0.12-2 ≤1->512 ≤0.06->16 0.5->32 ≤1->512 1->8 512->512 ≤0.06->16 32->32 ≤1-256 ≤0.12-0.5 4-32 0.12->16 0.5->32 ≤1->512 	NA 99.6 67.1 100° 86.9 77.2 0 83.4 93.0 49.2 NA 75.8 NA 75.8 NA 98.9 100 100 55.7 73.3 ^f 67.1	NA 0 9.0 - 8.3 - 16.9 0.7 2.8 37.1 NA 5.7 NA 5.7 NA 0 - 0 1.1	NA 0.4 23.9 0 4.8 22.8 83.1 15.9 4.2 13.7 NA 13.7 NA 18.5 NA 1.1 0 0 43.2 26.7 20.3	UD ^c 99.6 76.7 100 81.4 77.2 16.9 83.4 97.2 NA 97.2 NA 75.8 ^d NA 97.8 100 NA 97.8 100 NA 55.7 ^d NA	UD - 0 0.7 - 0.7 - 0.7 - NA NA NA NA - NA - NA - NA - NA - NA	UD 0.4 23.3 0 18.6 22.1 83.1 15.9 2.8 NA NA 24.2 NA 24.2 NA 24.2 NA 2.2 0 NA 44.3 NA 44.3 NA	 ^d % Susceptible in ^e AMC activity pressure f AMC activity pressure f AMC activity pressure sXT, trimethoprimapplicable. Table 2. MIC dissolation Table 2. MIC dissolation Table 2. MIC dissolation Genus/species (n <i>Escherichia coli (</i> <i>Escherichia pneum</i> <i>Klebsiella pneum</i> (23) <i>Enterococcus fae</i> <i>Proteus mirabilis</i> <i>Pseudomonas ae</i> (124) <i>Staphylococcus a</i> <i>Enterobacter cloa</i> <i>Klebsiella oxytoc</i> 	ncluded isolates cate edicted by testing an edicted by testing cell n-sulfamethoxazole; stributions for fost (2785) ≤ 11 (2785) ≤ 59.5 ESBL (196) 49.5 noniae (359) 0.3 noniae (359) 0.3 noniae-ESBL ecalis (333) $\leq (145) \qquad 9.0$ eruginosa 0.8 aureus (89) 6.7 acae (79) 8.9 $\approx (72) \qquad 1.4$	omycin omycin 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	r <i>E. faeca</i> <i>S. aureus</i> furantoin; against u 94.2 93.9 4.5 0.3 60.0 4.8 47.2	Alis. CIP, cipr CIP, cipr CIP, cipr Cumulativ 8 95.7 94.9 10.9 8.7 0.6 69.7 73.0 27.8 18.1	ofloxacin; AM ates collect osfomycin M <u>/e % of isolat</u> 16 97.2 95.9 95.9 95.9 940.5 1.8 75.2 8 10.5 10.5 10.5 10.5 10.5 10.5 10.5 10.5	IC, amc ed by C (µg/m es inhib 2 3.3 5.4 0.2 3.3 5.4 0.2 1.4 5.9 7.8 7.0 7.8	15 lab ited at 64 99.2 89.7 78.3 88.3 86.9 49.2 98.9 67.1 86.1	oratori MIC 128 99.8 98.5 94.2 87.0 98.5 95.2 86.3 79.7 95.8	es in C 250 99. 99. 96. 95. 99. 96. 95. 100 86. 98.	anada 6 9 0 9 7 4 6 2 0 1 6	51 2 100 100 100 100 100 100 100	
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¹University of Manitoba and ²Shared Health, Winnipeg, Canada

Results

omparative antimicrobial agents against outpatient urine	è
a from 2007 to 2019	

Table 1. In vitro activities of fosfomycin and comparative antimicrobial agents against outpatient urine isolates collected by 15 laboratories in Canada from 2007 to 2019 (Continued)



Dr. George G. Zhanel Department of Medical Microbiology Max Rady College of Medicine MS673-820 Sherbrook St. Winnipeg, MB R3A 1R9 Email: ggzhanel@pcsinternet.ca

Conclusions

- Fosfomycin demonstrated potent in vitro activity against *E. coli* with 99.2% of isolates susceptible and 96.4% of ESBL producing *E. coli*.
- 89.7% of *K. pneumoniae* were inhibited by fosfomycin when MICs were interpreted using *E. coli* breakpoints and 78.3 of ESBL producing K. pneumoniae.
- For other Enterobacterales, fosfomycin susceptibilities ranged from 67.1-100%.
- 49.2% of fosfomycin MICs for isolates of *P. aeruginosa* were susceptible when interpreted using *E. coli* breakpoints.
- 88.3% of *E. faecalis* were susceptible to fosfomycin.
- 98.9% of fosfomycin MICs for isolates of *S. aureus* were susceptible when MICs were interpreted using *E. coli* breakpoints.
- Our data are consistent with the literature which reports the antibacterial spectrum of fosfomycin includes the majority of enteric Gram-negative bacteria and that fosfomycin demonstrates higher MICs for Klebsiella, Enterobacter, and Serratia than for E. coli, Citrobacter, and Proteus (5).
- Fosfomycin demonstrated activity against *P. aeruginosa* in our study, with variable MICs ranging from ≤ 1 to $>512 \mu g/ml$, which is consistent with the literature (5).
- Acinetobacter spp. and Gram-negative anaerobic bacteria are not susceptible to fosfomycin (5).
- Our data are consistent with the literature which reports that fosfomycin is active versus Gram-positive cocci including S. aureus, S. pneumoniae and Enterococcus spp. (5). The majority of isolates of S. aureus, and enterococci (including VRE) have fosfomycin MICs ≤32 ug/ml. Some streptococci, Staphylococcus saprophyticus, corynebacteria, Chlamydia, and mycoplasmsas have been reported to be resistant to fosfomycin, likely due to the absence or low abundance of the MurA target (5).
- The difference in CLSI and EUCAST MIC breakpoints appears to impact the % of isolates of Enterobacterales from urine reported as susceptible.
- In general, fosfomycin possesses broad-spectrum activity against most Gram-negative and Gram-positive bacterial pathogens causing urinary tract infections.

Acknowledgements

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