In vitro Evaluation of Delafloxacin Activity when Tested against **Contemporary Isolates from European Acute Skin and Skin** Structure Infections: Results from the SENTRY Antimicrobial Surveillance Program (2018–2020)

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# Introduction

- Delafloxacin is a broad-spectrum anionic fluoroquinolone antibacterial with activity against Gram-positive and Gramnegative organisms.
- Delafloxacin is approved by the FDA and EMA in adults for use in the treatment of acute bacterial skin and skinstructure infections (SSSIs) and community-acquired bacterial pneumonia
- In this study, the in vitro susceptibility of delafloxacin and comparator quinolones levofloxacin, moxifloxacin, and ciprofloxacin (for *E. coli*) were determined for recent clinical isolates from SSSI collected at the 37 medical centres in Europe participating in the SENTRY Surveillance Program during 2018–2020.

# Materials and Methods

- A total of 8,277 SSSI isolates were consecutively collected and included only 1 isolate per patient per infection episode.
- Isolate identification was determined at each site and confirmed using standard biochemical or molecular methods at JMI Labs.
- Susceptibility testing was performed according to CLSI broth microdilution methodology, and CLSI and EUCAST (2021) interpretive criteria were applied.
- An arbitrary susceptible breakpoint of  $\leq 0.001 \text{ mg/L}$  was published by EUCAST for levofloxacin when tested against staphylococci and streptococci, indicating that susceptible should not be reported for this organism-agent combination, and intermediate should be interpreted as susceptibleincreased exposure.

# Results

- The frequencies of the most common organisms isolated from SSSI are shown in Figure 1.
- Staphylococcus aureus was the most common pathogen encountered in SSSI (n=3,130). – Among this species, 83.5% of the isolates were methicillinsusceptible (MSSA) and 16.5% were methicillin-resistant (MRSA).
- Escherichia coli was the second most common species (n=945) isolated, and *P. aeruginosa* was third.
- common pathogen. . Included in this group were: Streptococcus agalactiae (n= 140), S. canis (n= 2), S. dysgalactiae (177), S. pyogenes (n=277)
- The susceptibility results for delafloxacin and the quinolone comparators for the most common species having delafloxacin breakpoints are shown in Table 1.
- Delafloxacin was the most potent quinolone tested based on MIC, value. The MIC distributions of delafloxacin and comparators for the indicated species are shown in Table 2 for Gram-positive organisms and *E. coli* is shown in Table 3.
- Delafloxacin had the highest percent susceptibility against S. aureus overall (93.1%) as well as against MSSA (98.7%) and MRSA (64.9%).
- The  $\beta$ -haemolytic streptococci were >98% susceptible to delafloxacin and moxifloxacin.
- Levofloxacin had no susceptible Gram-positive isolates with EUCAST criteria, 85.9% of S. aureus and 98.7% of streptotoccoci were categorized as susceptible-increased exposure, intermediate.
- E. coli susceptibility ranged from 67.8% for levofloxacin to 59.0% for delafloxacin.

# Conclusions

- Delafloxacin had potent activity against recent SSSI isolates from European hospitals.
- Delafloxacin had the highest susceptibility of the quinolones tested against S. aureus, including MRSA and MSSA and had high susceptibility to  $\beta$ -haemolytic streptococci.
- These in vitro results suggest that delafloxacin may be a useful therapy for SSSI caused by Gram-positive and susceptible Gram-negative isolates in Europe.

– As a group,  $\beta$ -haemolytic streptococci were the fourth most

# structure infection

			mg/L			CLSI <sup>a</sup>			<b>EUCAST</b> <sup>a</sup>	
Antimicropial agent	NO. OT ISOIATES	MIC <sub>50</sub>	MIC <sub>90</sub>	MIC range	% <b>S</b>	%	% <b>R</b>	% <b>S</b>	%	% <b>R</b>
S. aureus										
Delafloxacin	3,130	0.004	0.25	≤0.0005 to 8	93.1 <sup>b,c</sup> 88.4 <sup>d,e</sup>	4.1 4.7	2.7 6.9	93.1		6.9
Levofloxacin	3,130	0.25	>4	≤0.03 to >4	85.9	0.2	13.9	f	85.9	14.1
Moxifloxacin	3,130	≤0.06	2	≤0.06 to >4	86.1	1.0	12.9	86.0		14.0
MSSA										
Delafloxacin	2,614	0.004	0.008	≤0.0005 to 2	98.7 <sup>b,c</sup> 97.1 <sup>d,e</sup>	0.8 1.6	0.5 1.3	98.7		1.3
Levofloxacin	2,614	0.25	0.25	≤0.03 to >4	96.1	0.2	3.7	f	96.1	3.9
Moxifloxacin	2,614	≤0.06	≤0.06	≤0.06 to >4	96.3	0.5	3.3	96.2		3.8
MRSA										
Delafloxacin	516	0.25	1	0.002 to 8	64.9 <sup>b,c</sup> 44.4 <sup>d,e</sup>	20.9 20.5	14.1 35.1	64.9		35.1
Levofloxacin	516	>4	>4	0.12 to >4	33.9	0.6	65.5	f	33.9	66.1
Moxifloxacin	516	2	>4	≤0.06 to >4	34.7	3.7	61.6	34.1		65.9
β-haemolytic streptococci <sup>g</sup>										
Delafloxacin	596	0.008	0.015	≤0.002 to 1	99.0 b,c	0.3	0.7	98.3		1.7
Levofloxacin	596	0.5	1	≤0.06 to >4	98.7	0.0	1.3	0.0	98.7	1.3
Moxifloxacin	596	0.12	0.25	≤0.03 to 4				98.7		1.3
E. coli										
Delafloxacin	945	0.06	4	≤0.004 to >16	64.1 <sup>b,c</sup> 64.1 <sup>d,e</sup>	1.0 1.0	34.9 34.9	59.0		41.0
Levofloxacin	945	0.06	16	≤0.015 to >32	67.8	1.1	31.1	67.8	1.1	31.1
Ciprofloxacin	943	≤0.03	>4	≤0.03 to >4	64.9	2.7	32.4	64.9	2.7	32.4
Moxifloxacin	945	≤0.06	16	≤0.06 to >16				59.8		40.2
Criteria as published by CLSI (202 Using FDA ABSSSI breakpoints US FDA breakpoints were applied.	1) and EUCAST (2021)									

- <sup>d</sup> Using FDA CABP breakpoints <sup>e</sup> US FDA breakpoints published for MSSA isolates were applied to all Staphylococcus aureus isolates
- <sup>g</sup>Organisms include: Streptococcus agalactiae (140), S. canis (2), S. dysgalactiae (177), S. pyogenes (277)

### Table 2. MIC distributions of delafloxacin and comparators for Gram-positive isolates in this study

		Number and cumulative percent at MIC (mg/L)														
Antimicropial Agent	0.002	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	>		
MSSA (n=2614)							1									
Delefleveein	496	1261	659	47	7	2	20	42	21	12	1				0.004	0.000
Delanoxacin	20.7%	69.0%	94.2%	96.0%	96.3%	96.3%	97.1%	98.7%	99.5%	>99.9%	100.0%					800.0
					1	18	827	1559	89	19	4	17		80	0.25	0.25
Levonoxacin					<0.1%	0.7%	32.4%	92.0%	95.4%	96.1%	96.3%	96.9%		100.0%		
Moviflovooin						2368	136	11	1	12	49	16		21	≤0.06	
IVIOXITIOXACIN						90.6%	95.8%	96.2%	96.3%	96.7%	98.6%	99.2%		100.0%		20.00
MRSA (n=516)																
Doloflovacin	32	90	49	8	1	6	43	106	108	45	8	13	7		0.25	1
Delanoxacin	6.2%	23.6%	33.1%	34.7%	34.9%	36.0%	44.4%	64.9%	85.9%	94.6%	96.1%	98.6%	100.0%			
Lovoflovocin						0	51	103	17	4	3	37		301	>4	>4
Levonoxacin						0.0%	9.9%	29.8%	33.1%	33.9%	34.5%	41.7%		100.0%		
Moviflovocin						154	21	1	3	19	111	115		92	2	>4
WIUXIIIUXACIII						29.8%	33.9%	34.1%	34.7%	38.4%	59.9%	82.2%		100.0%		
β-haemolytic streptococci (n=	596)															
Doloflovooin	9	77	245	230	25	4	2	1	2	1					0.008	0.015
Delanoxacin	1.5%	14.4%	55.5%	94.1%	98.3%	99.0%	99.3%	99.5%	99.8%	100.0%						CTO'O
Lovoflovooin					1	0	46	374	152	15	0			8	0.5	1
Levonoxacin					0.2%	0.2%	7.9%	70.6%	96.1%	98.7%	98.7%			100.0%		
Moviflovooin				3	74	379	128	4	1	3	4				0 1 2	0.25
Ινιυλπιυλασπι				0.5%	12.9%	76.5%	98.0%	98.7%	98.8%	99.3%	100.0%				U.12	0.20
EUCAST breakpoints- susceptible, gre	en; susceptible-in	creased expo	sure intermed	liate, yellow; r	esistant, red											

### Table 3. MIC distributions of delafloxacin and comparators for E. coli (n=945)

<b>Antimicrobial Agent</b>		Number and cumulative percent at MIC (mg/L)														
	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	>	Iotal	
	9	106	317	80	45	48	9	25	114	118	43	10		20		
Delafloxacin	1.1%	12.3%	45.8%	54.3%	59.0%	64.1%	65.1%	67.7%	79.8%	92.3%	96.8%	97.9%		100.0%	945	0.0
		50	411	51	8	56	65	10	6	26	97	117	38	10		
Levofloxacin		5.3%	48.8%	54.2%	55.0%	61.0%	67.8%	68.9%	69.5%	72.3%	82.5%	94.9%	98.9%	100.0%	945	0.0
			506	13	31	62	25	12	5	11				278		
Ciprofloxacin			53.7%	55.0%	58.3%	64.9%	67.6%	68.8%	69.4%	70.5%				100.0%	943	≤0.0
				495	24	46	51	30	6	14	46	139		94		
Moxifloxacin				52.4%	54.9%	59.8%	65.2%	68.4%	69.0%	70.5%	75.3%	90.1%		100.0%	945	≤ <b>0.</b> C
EUCAST breakpoints- susceptible, gr	reen; intermediate,	yellow; resis <sup>.</sup>	tant, red													

### Table 1. Susceptibilities of delafloxacin and comparators tested against isolates from acute bacterial skin and skin

An arbitrary susceptible breakpoint of  $\leq 0.001$  mg/L and/or >50 mm has been published by EUCAST indicating that susceptible should not be reported for this organism-agent combination and intermediate should be interpreted as susceptible increased

### Figure 1. Most common organisms isolated from SSSI



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