

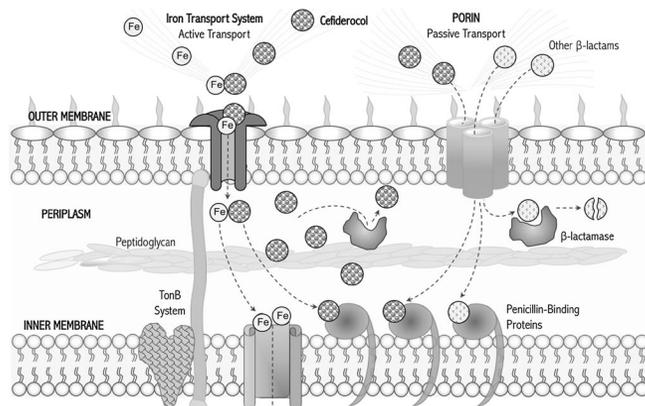
Introduction

- Cefiderocol is a novel cephalosporin recently approved by the FDA for treatment of multidrug-resistant urinary tract infections. It has demonstrated in vitro activity against aerobic Gram-negative bacteria, including carbapenem-resistant *Enterobacteriaceae*, *Pseudomonas aeruginosa*, *Acinetobacter* species, and *Stenotrophomonas maltophilia*
- Michigan Medicine utilizes custom Trek Sensititre broth microdilution panels, which allows the choice of antimicrobials and dilution ranges tailored their formulary requirements.
- Susceptibility and interpretative criteria were based on 2019 CLSI M100 breakpoints: ≤ 4 S, 8 I, ≥ 16 R.

Mechanism of Action

Cefiderocol remains effective despite the 3 main mechanisms of Gram-negative bacterial resistance to Beta lactam drugs

- Changes in porin channels
- Beta lactamases
- Overexpression of efflux pumps.

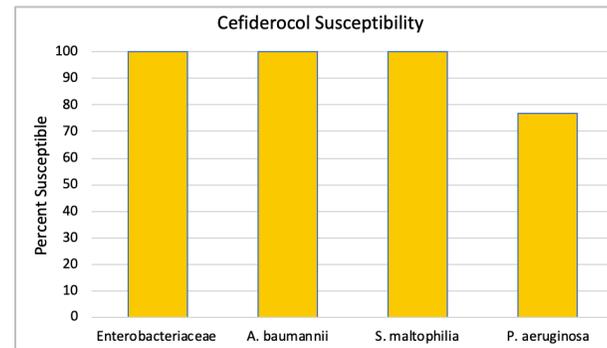


Cefiderocol belongs to a class of drugs called siderophore cephalosporins. It binds to free iron and is transported into the bacterial cell, preventing cell wall synthesis once inside.

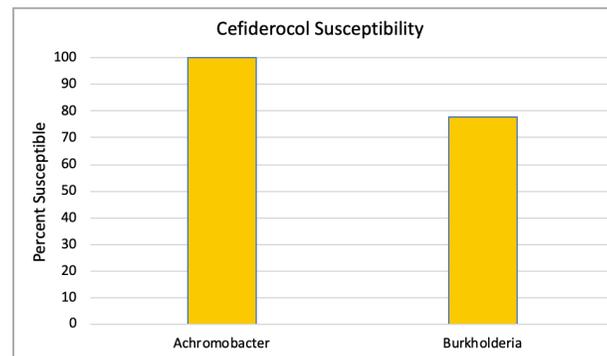
Methods

Broth microdilution for cefiderocol requires iron-depleted cation adjusted Mueller-Hinton broth. Iron-depleted media imitates physiological iron concentration and better correlates with in vitro susceptibility.

We tested 100 clinical isolates consisting of *Enterobacteriales* (n=41) and non-fermenting gram negative bacilli (59): *P. aeruginosa* (n=13), *Burkholderia* (9), *Achromobacter* (15), *S. maltophilia* (7), *Enterobacter* (6), *Klebsiella* (9), *Escherichia coli* (10), *Serratia* (6), *Proteus* (5), *Morganella* (1), *Acinetobacter baumannii* (15), and *Citrobacter* (4).



- CLSI currently has no breakpoints for *Achromobacter* and *Burkholderia*.
- All 15 isolates of *Achromobacter* had an MIC of < 2 ug/mL.
- 7 of 9 *Burkholderia* isolates had an MIC of < 2 ug/mL. 2 *Burkholderia* had an MIC of 32 ug/mL and would presumably be resistant.



Conclusions

- Cefiderocol demonstrated excellent in vitro activity against members of the *Enterobacteriales* group, *A. baumannii*, *Achromobacter spp.* and *S. maltophilia*. Susceptibility was reduced for both *P. aeruginosa* and *Burkholderia spp.*
- Addition of newly approved antimicrobials to commercially available antimicrobial susceptibility panels may take a year or longer. By custom designing and validating research use only panels, our laboratory at Michigan Medicine allow us to test new antimicrobials as soon as they are approved for testing by the FDA.
- Cefiderocol has been added to our panels for routine testing of *Enterobacteriales* and non-fermentative Gram-negative bacilli.

Non-Fermenter Panel

	1	2	3	4	5	6	7	8	9	10	11	12
A	GEN	GEN	GEN	GEN	TOB	TOB	TOB	IM	IM	IM	IM	IM
B	AS2	AS2	AS2	TCC	TCC	MN	MN	MN	DOX	DOX	DOX	DOX
C	CT	CT	CT	CT	CT	MR	MR	MR	MR	MR	MR	MR
D	MERO	MERO	MERO	MERO	CIP	CIP	CIP	CIP	SXT	SXT	SXT	SXT
E	CZA	CZA	CZA	CZA	FEP	FEP	FEP	FEP	POS	POS	POS	POS
F	FUR	FUR	FUR	LEVO	LEVO	LEVO	LEVO	LEVO	COL	COL	COL	COL
G	AZI	AZI	AZI	TAZ	TAZ	MEV	MEV	MEV	MEV	POS	POS	POS
H	AMI	AMI	AMI	AMI	PIT4	PIT4	PIT4	PIT4	POS	POS	POS	POS

Gram-negative Panel

	1	2	3	4	5	6	7	8	9	10	11	12
A	TOB	TOB	TOB	GEN	GEN	AS2	AS2	AZI	AZI	TCC	TCC	TCC
B	FOS+	FOS+	FAZ	FAZ	FAZ	AMP	AMP	AUG2	AUG2	NIT	NIT	NIT
C	PIT4	PIT4	PIT4	PIT4	FEP	FEP	FEP	MERO	MERO	MERO	CZA	CZA
D	ETP	ETP	ETP	MEV	MEV	MEV	FDC	FDC	FDC	FDC	FDC	FDC
E	AM	AM	AM	CIP	CIP	CIP	CIP	COL	COL	SXT	SXT	SXT
F	FUR	FUR	FUR	LEVO	LEVO	LEVO	MR	MR	MR	MR	POS	POS
G	FOT	FOT	FOT	FOT	FIC	FIC	FIC	FIC	FIC	FIC	FIC	FIC
H	TAZ	TAZ	TAZ	TAZ	TIC	TIC	TIC	TIC	TIC	TIC	TIC	TIC

References

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