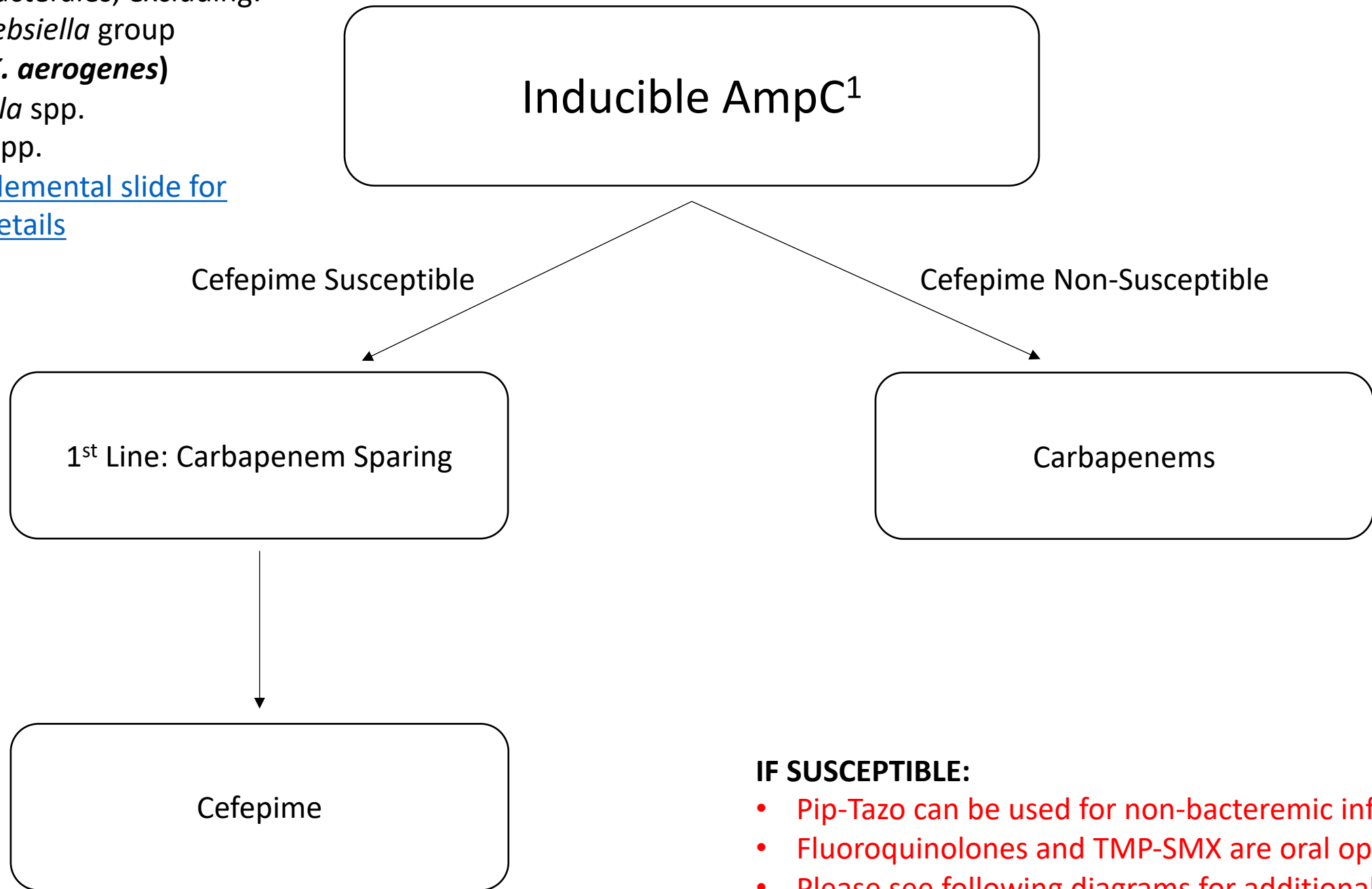


Drug Resistant Gram-Negative Organisms

Carbapenemases	β -lactamases
<u>OXA-48</u>	<u>Inducible AmpC</u>
<u>KPC</u>	<u>Ceftriaxone Resistance/CTX-M</u>
<u>NDM</u> & <u>VIM/IMP</u>	
	Appendices
Other Organisms	<u>Organism Group Definitions</u>
<u>DTR <i>Pseudomonas</i></u>	<u>Combination Therapies</u>
<u>CR <i>Acinetobacter baumannii</i></u>	<u>Dosing Table 1, Table 2 & Table 3</u>
<u><i>Stenotrophomonas maltophilia</i></u>	<u>Common Acronyms</u>

¹All Enterobacterales, excluding:

- *E. coli*/Klebsiella group
(except *K. aerogenes*)
- *Salmonella* spp.
- *Shigella* spp.
- [See supplemental slide for further details](#)



IF SUSCEPTIBLE:

- Pip-Tazo can be used for non-bacteremic infection
- Fluoroquinolones and TMP-SMX are oral options
- Please see following diagrams for additional resistance

Ceftriaxone Resistance/CTX-M¹

Bacteremia or Severe Infection

Carbapenems

Non-Severe

Piperacillin-Tazobactam

OR

TMP-SMX³

OR

Fluoroquinolones³

Cystitis²

1st: Nitrofurantoin

OR

1st: TMP-SMX³

OR

2nd: Amoxicillin-Clavulanate

OR

3rd: [Single Dose Aminoglycoside](#)

¹[E. coli/Klebsiella group \(except K. aerogenes\)](#)

²[Fosfomycin](#) can also be used for susceptible *E. coli* cystitis

³May be used as step-down for severe infection if susceptible following source control

NOTE: Please see following diagrams for additional resistance

OXA-48

1st Line

2nd Line

3rd Line

[Ceftazidime-Avibactam](#)¹

[Cefiderocol](#)¹

[Plazomicin](#)^{1,2,3}

OR

[Tigecycline](#)^{2,4} / [Eravacycline](#)^{2,3,4}

¹Limited anaerobic activity

²Use as part of combination therapy and not for bacteremia

³Non-formulary

⁴Avoid for UTIs

KPC

1st Line

2nd Line

3rd Line

Ceftazidime-Avibactam¹

Cefiderocol¹

Plazomicin^{1,2,3}

OR

OR

Meropenem-Vaborbactam³ /
Imipenem-Relebactam³

Tigecycline^{2,4} / Eravacycline^{2,3,4}

¹Limited anaerobic activity

²Use as part of combination therapy and not for bacteremia

³Non-formulary

⁴Avoid for UTIs

MBL¹

Preferred

Alternative

1st: Ceftazidime-Avibactam + Aztreonam²

Tigecycline³ / Eravacycline^{3,4}

OR

2nd: Cefiderocol²

¹NDM and VIM/IMP

²Limited anaerobic activity

³Use as part of combination therapy and not for bacteremia or UTI

⁴Non-formulary

DTR *Pseudomonas*

Preferred

Alternative

Alternative (Cystitis Only)

1st: [Ceftolozane-Tazobactam](#)^{1,2}

OR

2nd: [Ceftazidime-Avibactam](#)²

OR

3rd: [Cefiderocol](#)²

[Imipenem-Relebactam](#)³

OR

[Daily Aminoglycoside](#)^{2,4}

OR

[Polymyxin B](#)^{2,4}

[Single Dose Aminoglycoside](#)

OR

[Colistin](#)

¹Highest percentage of isolates are susceptible to this antibiotic

²Limited anaerobic activity

³Non-formulary

⁴Use in combination with a preferred novel β -lactam agent. Polymyxin B is for infections outside the urinary tract

Carbapenem-Resistant
Acinetobacter baumannii

Bacteremia / Moderate-Severe Infection

Mild Infection

[High Dose Ampicillin-Sulbactam](#)¹

[Ampicillin-Sulbactam](#)

OR

OR

[Combination Therapy](#)²

[Minocycline](#)³ > [Tigecycline](#)³

¹Can use as part of combination therapy if with documented resistance

²Please see appendix for possible combination therapies

³High dose, see supplemental dosing table for details

Stenotrophomonas maltophilia

Bacteremia / Moderate-Severe Infection

Combination Therapy¹

OR

Ceftazidime-Avibactam +
Aztreonam²

Mild Infection

1st: TMP-SMX

OR

2nd: Levofloxacin

OR

2nd: Minocycline³ > Tigecycline³

OR

3rd: Cefiderocol

¹Please see appendix for possible combination therapies

²Suggested when neither TMP-SMX nor Minocycline are considered viable treatment options

³High dose, see supplemental dosing table for details

NOTE: Ceftazidime should not be used, even if susceptible

Appendix: Organism Group Definitions

<u>E. coli/Klebsiella Group (No Inducible AmpC)</u>	<u>Inducible AmpC¹</u>
<i>Citrobacter koseri</i>	All Enterobacterales, excluding: <ul style="list-style-type: none"> - <i>E. coli/Klebsiella</i> group (see left) - <i>Salmonella</i> spp. - <i>Shigella</i> spp.
<i>Citrobacter amalonaticus</i> group (<i>C. amalonaticus</i> , <i>C. farmeri</i> , <i>C. sedlakii</i>)	
<i>Escherichia</i> spp.	
<i>Klebsiella oxytoca</i>	
<i>Klebsiella pneumoniae</i>	
<i>Klebsiella variicola</i>	
Other <i>Klebsiella</i> spp. (except <i>K. aerogenes</i>)	
<i>Proteus mirabilis</i>	
<i>Raoultella</i> spp.	

¹Moderate to high risk for clinically significant inducible AmpC include: *Enterobacter cloacae*, *Klebsiella aerogenes*, and *Citrobacter freundii*

Appendix: Combination Therapies

CRAB

At least two of the following:

- [Ampicillin-Sulbactam](#)¹
- [Meropenem](#)²
- [Cefiderocol](#)
- [Minocycline](#)¹ > [Tigecycline](#)¹
- [Polymyxin B](#)³ / [Colistin](#)⁴

Stenotrophomonas maltophilia

At least two of the following:

- [TMP-SMX](#)
- Levofloxacin
- [Cefiderocol](#)
- [Minocycline](#)¹ > [Tigecycline](#)¹

¹High dose

²High dose extended infusion

³For infections outside the urinary tract

⁴For infections isolated to the urinary tract

Appendix: Suggested Dosing Table 1

Agent	Adult Dosage (assuming normal renal and liver function)	Pediatric Dosage (do not exceed adult dosing)
Aminoglycosides ¹	<p>Amikacin Cystitis: 15 mg/kg IV x1 All other infections: 20 mg/kg IV x1, subsequent dosing per PK</p> <p>Gentamicin Cystitis: 5 mg/kg IV x1 All other infections: 7 mg/kg IV x1, subsequent dosing per PK</p> <p>Plazomicin² Cystitis: 15 mg/kg IV x1 All other infections: 15 mg/kg IV x1, subsequent dosing per PK</p> <p>Tobramycin Cystitis: 5 mg/kg IV x1 All other infections: 7 mg/kg IV x1, subsequent dosing per PK</p>	
Ampicillin-Sulbactam	<p>Moderate/Severe (CRAB): 9 g IV q8h over 4 hours</p> <p>Mild (CRAB): 3 g IV q4h</p>	<p>CRAB: 400 mg/kg/day divided q6h; if moderate/severe, infuse over 4 hours</p>

¹Use adjusted body weight for aminoglycosides in obese patients

²Not available for pediatric populations

Appendix: Suggested Dosing Table 2

Agent	Adult Dosage (assuming normal renal and liver function)	Pediatric Dosage (do not exceed adult dosing)
Cefiderocol	2 g IV q8h, infuse over 3 hours; for CrCl >120, can increase to 2g IV q6h, infuse over 3 hours	60 mg/kg IV q8h, infuse over 3 hours
Ceftazidime-Avibactam	2.5 g IV q8h, infuse over 3 hours	50 mg/kg (CAZ) IV q8h, infuse over 3 hours
Ceftazidime-Avibactam and Aztreonam	CAZ-AVI: 2.5 g IV q8h, infuse over 3 hours <u>PLUS</u> Aztreonam: 2 g IV q8h, infuse over 3 hours and administer at same time as CAZ-AVI	CAZ-AVI: 50 mg/kg (CAZ) IV q8h, infuse over 3 hours <u>PLUS</u> Aztreonam: 30 mg/kg IV q6h, infuse over 3 hours and administer at same time as CAZ-AVI
Ceftolozane-Tazobactam	Cystitis: 1.5 g IV q8h, infuse over 1 hour All other infections: 3 g IV q8h, infuse over 3 hours	Cystitis: 20 mg/kg (TOL) IV q8h, infuse over 1 hour All other infections: 40 mg/kg (TOL) IV q8h, infuse over 3 hours
Colistin / Polymyxin B	Refer to international consensus guidelines on polymyxins	
Eravacycline	1 mg/kg IV q12h	**Not established** ≥ 8 years: 1.5 – 1.75 mg/kg studied in Phase 1 trials

Appendix: Suggested Dosing Table 3

Agent	Adult Dosage (assuming normal renal and liver function)	Pediatric Dosage (do not exceed adult dosing)
Fosfomycin	Cystitis (<i>E. coli</i>): 3 g PO x1	Cystitis (<i>E. coli</i>): 1-12 months: 1 g PO x 1; 1-18 years: 2g PO x 1
Imipenem- Relebactam	1.25 g IV q6h, infuse over 30 minutes	15 mg/kg (IMI) IV q6h, infuse over 30 minutes
Meropenem	CRE/CRAB: 2 g IV q8h, infuse over 3 hours	CRE/CRAB: 40 mg/kg IV q8h, infuse over 3 hours
Meropenem- Vaborbactam	4 g IV q8h, infuse over 3 hours	40 mg/kg (MEM) IV q8h, infuse over 3 hours
Minocycline	High dose: 200 mg PO q12h	High dose: 4 mg/kg PO q12h
Tigecycline	High dose: 200 mg IV x1, then 100 mg IV q12h	High dose: 4 mg/kg IV x1, then 2-3.2 mg/kg IV q12h
Trimethoprim- Sulfamethoxazole	<i>S. maltophilia</i>: 8 - 12 mg/kg/day (TMP) IV/PO divided q12h	<i>S. maltophilia</i>: 15-20 mg/kg/day (TMP) IV/PO divided q6-8h, okay to exceed adult dosing

Common Acronyms

General Terms

CRAB: carbapenem-resistant *Acinetobacter baumannii*

CRE: carbapenem-resistant Enterobacterales

DTR: difficult-to-treat resistance¹

MBL: metallo- β -lactamase

XDR: extensively drug resistant²

Antibiotics

AVI: Avibactam

CAZ: Ceftazidime

IMI: Imipenem

MEM: Meropenem

TOL: Ceftolozane

TMP: Trimethoprim

¹Non-susceptible to fluoroquinolones and all β -lactam categories, including carbapenems

²Non-susceptible to all but ≤ 2 classes of antibiotics; if intermediate or resistant to any antibiotic within a class, then considered resistant to entire class