Drug Name	**Ceftolozane/tazobactam**
Brand Name(s)	Zerbaxa®
Drug Class	Beta lactam (Cephalosporin) with beta lactamase inhibitor
Restriction level	**ID consult required**

Accepted Indications	- Management of infections due to multi-drug resistant (MDR) *Pseudomonas* species resistant to alternative agents including carbapenems
	  ○ Complicated intraabdominal infection (cIAI) with metronidazole
	  ○ Complicated urinary tract infection (cUTI)
	  ○ Nosocomial/healthcare associated pneumonia

Unacceptable Uses	- Empiric treatment of cIAI or cUTI without high suspicion for MDR *Pseudomonas* resistant to alternative agents including carbapenems
Side Effects	- Caution if history of hypersensitivity/anaphylactic reaction to other beta lactam antibiotics - Nausea - Headache - Diarrhea
Pregnancy Class	B
Dosing	cIAI, cUTI: 1.5g IV q8h Pneumonia: 3g IV q8h Renal dosing: - CrCl 30-50 mL/min: 750mg dose IV q8h - CrCl 15-29 mL/min: 375mg dose IV q8h - ESRD on HD: loading dose 750mg IV then 150mg IV q8h, administer after HD at earliest possible time
Lab monitoring	Susceptibility testing must be requested from the Microbiology lab Chem8 *at least* weekly

Questions to ask prior to approval:

- Does the patient have an active, culture proven infection or a high suspicion (i.e. recent prior culture positive in the past six months) of an infection with multi-drug, carbapenem resistant Pseudomonas?
- Does the case match one of the Accepted Indications?

Answer of “no” to any of the above questions should prompt evaluation for an alternative therapy.

Formal consultation with Infectious Diseases is required.

Susceptibility testing must be requested from Microbiology lab.

Background:

Ceftolozane-tazobactam is a cephalosporin β-lactam and β-lactamase inhibitor combination approved in the United States for the treatment of complicated urinary tract and intraabdominal infections in combination with metronidazole. Ceftolozane is a novel cephalosporin that is similar in structure to ceftazidime. Ceftolozane is a bactericidal agent as a result of the inhibition of bacterial cell wall synthesis mediated by penicillin-binding proteins (PBPs). It has expansive coverage against gram negative organisms, and it has high affinity to PBPs important in *P. aeruginosa.* As ceftolozane is hydrolyzed by extended spectrum beta-lactamases, it is paired with tazobactam to broaden its antibacterial activity. Ceftolozane has limited activity against anaerobes and is used with metronidazole in the treatment of intraabdominal infections.

US Food and Drug Administration interpretive criteria (µg/mL)			
	Enterobacteriaceae	*Pseudomonas aeruginosa*	*Bacteroides fragilis*
Susceptible	≤2/4	≤4/4	≤8/4
Intermediate	4/4	8/4	16/4
Resistant	≥8/4	≥16/4	≥32/4

In the phase 3 clinical studies, no statistically significant adverse events were noted compared to its comparator agents. Most common side effects include nausea, headache, diarrhea, pyrexia, constipation, insomnia, and vomiting. Increases in liver transaminases were the most common laboratory reaction, but this was not significantly different from the comparator agents. No significant drug-drug interactions were observed in the clinical trials.

Ceftolozane-tazobactam is currently being studied to establish its efficacy in ventilator associated bacterial pneumonia. The dosing is this Phase 3 study utilizes a high dose of 3g IV q8h.

Reference:

1. Cosgrove SE *et al. John Hopkins Antibiotic Guidelines*
2. Zerbaxa®, Merck and Co., Inc., New Jersey, USA; 2015. https://www.merck.com/product/usa/pi_circulars/z/zerbaxa/zerbaxa_pi.pdf
3. Solomkin J *et al. Clin Infect Dis* 2015; 60(10): 1462-71
4. Wagenleher FM *et al. Lancet* 2015; 385(9981): 1949-56
5. Cluck D *et al. Am J Health Syst Pharm* 2015; 72(24): 2135-2146