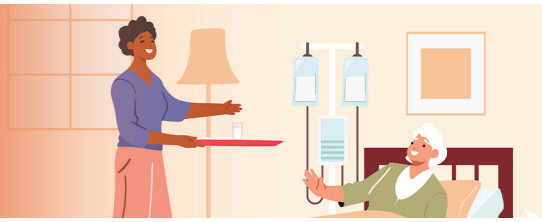
ZERBAXA®
ceftolozane and tazobactam
for injection

Consider Utilization of ZERBAXA in OUTPATIENT Settings[1]



Indications for ZERBAXA

ZERBAXA is indicated for the treatment of adult patients (18 years and older) with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP), caused by the following susceptible Gram-negative microorganisms: *Enterobacter cloacae, Escherichia coli, Haemophilus influenzae, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa,* and *Serratia marcescens.*

ZERBAXA is indicated for the treatment of adult and pediatric patients (birth to less than 18 years old) with complicated urinary tract infections (cUTI), including pyelonephritis, caused by the following susceptible Gram-negative microorganisms: *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis,* and *Pseudomonas aeruginosa.*

ZERBAXA used in combination with metronidazole is indicated for the treatment of adult and pediatric patients (birth to less than 18 years old) with complicated intra-abdominal infections (cIAI) caused by the following susceptible Gram-negative and Gram-positive microorganisms: *Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Bacteroides fragilis, Streptococcus anginosus, Streptococcus constellatus,* and *Streptococcus salivarius.*

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of ZERBAXA and other antibacterial drugs, ZERBAXA should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Important Safety Information for ZERBAXA

- **Patients with renal impairment:** Decreased efficacy of ZERBAXA has been observed in patients with baseline CrCl of 30 to ≤50 mL/min. In a clinical trial of adult patients, patients with cIAIs with CrCl >50 mL/min had a clinical cure rate of 85.2% when treated with ZERBAXA plus metronidazole vs 87.9% when treated with meropenem. In the same trial, patients with CrCl 30 to ≤50 mL/min had a clinical cure rate of 47.8% when treated with ZERBAXA plus metronidazole vs 69.2% when treated with meropenem. A similar trend was also seen in the cUTI trial. Dose adjustment is required for adult patients with CrCl 50 mL/min or less. All doses of ZERBAXA are administered over 1 hour. Monitor CrCl at least daily in patients with changing renal function and adjust the dose of ZERBAXA accordingly.
- **Hypersensitivity:** ZERBAXA is contraindicated in patients with known serious hypersensitivity to the components of ZERBAXA (ceftolozane/tazobactam), piperacillin/tazobactam, or other members of the beta-lactam class. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-lactam antibacterials. Before initiating therapy with ZERBAXA, make careful inquiry about previous hypersensitivity reactions to cephalosporins, penicillins, or other beta-lactams. If an anaphylactic reaction to ZERBAXA occurs, discontinue use and institute appropriate therapy.
- ***Clostridioides difficile*-associated diarrhea (CDAD),** ranging from mild diarrhea to fatal colitis, has been reported with nearly all systemic antibacterial agents, including ZERBAXA. Careful medical history is necessary because CDAD has been reported to occur more than 2 months after the administration of antibacterial agents. If CDAD is confirmed, antibacterial use not directed against *C. difficile* should be discontinued, if possible.

Important Safety Information for ZERBAXA continues on page 2.

Utilization of ZERBAXA® (ceftolozane and tazobactam) in inpatient and outpatient health care settings[1]

Inpatient utilization[a]:

71%

APPROXIMATELY 29%

of the utilization of ZERBAXA occurs in an outpatient facility[1]

Home infusion/ other:

16%

Hospital-affiliated infusion center:

8%

Physician office infusion center/other outpatient:

5%

[a]Total inpatient health care facilities consisted of hospital inpatient, long-term acute care, and nursing homes.[1]

Drug stability is an important consideration when selecting an antimicrobial for outpatient use[2]

24 HOURS
Room temperature stability of ZERBAXA in a suitable infusion bag

7 DAYS
Stability under refrigeration of ZERBAXA in a suitable infusion bag: 2°C to 8°C (36°F to 46°F)

Upon constitution with sterile water for injection or 0.9% sodium chloride injection, reconstituted solution of ZERBAXA may be held in the vial for 1 hour prior to transfer and dilution of the solution (with 0.9% of sodium chloride or 5% dextrose) in a suitable infusion bag.

Following dilution of the solution with 0.9% sodium chloride or 5% dextrose, ZERBAXA is stable for 24 hours when stored at room temperature or 7 days when stored under refrigeration at 2°C to 8°C (36°F to 46°F). Discard unused portion.

- Constituted ZERBAXA solution or diluted ZERBAXA infusion should not be frozen.

Important Safety Information for ZERBAXA *(continued)*

- **Development of drug-resistant bacteria:** Prescribing ZERBAXA in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and risks the development of drug-resistant bacteria.
- **Adverse reactions in adult patients with HABP/VABP:** The most common adverse reactions occurring in ≥5% of adult patients receiving ZERBAXA in the HABP/VABP trial were hepatic transaminase increased (11.9%), renal impairment/renal failure (8.9%), and diarrhea (6.4%).
- **Adverse reactions in adult patients with cIAI or cUTI:** The most common adverse reactions occurring in ≥5% of adult patients receiving ZERBAXA in the cUTI and cIAI trials were headache (5.8%) in the cUTI trial, and nausea (7.9%), diarrhea (6.2%), and pyrexia (5.6%) in the cIAI trial.
- **Adverse reactions in pediatric patients with cIAI or cUTI:** The most common adverse reactions occurring in ≥7% of pediatric patients receiving ZERBAXA in the cIAI trial were diarrhea (17%), thrombocytosis (16%), pyrexia (13%), abdominal pain (11%), vomiting (10%), increased aspartate aminotransferase (7%), and anemia (7%). The most common adverse reactions occurring in ≥7% of pediatric patients receiving ZERBAXA in the cUTI trial were thrombocytosis (9%), leukopenia (8%), diarrhea (7%), and pyrexia (7%).

Important Safety Information for ZERBAXA continues on page 3.

Dosing: ZERBAXA® (ceftolozane and tazobactam) is infused over a 1-hour period

Dosage of ZERBAXA by infection in adult patients (18 years and older) with CrCl[a] >50 mL/min

Infection	Dose	Frequency	Infusion Time	Duration
cUTI, including pyelonephritis	1.5 g	Every 8 hours	**1 hour**	7 days
cIAI[b]	1.5 g	Every 8 hours	**1 hour**	4 to 14 days
HABP/VABP	3 g	Every 8 hours	**1 hour**	8 to 14 days

Dosage of ZERBAXA in adult patients with renal impairment (CrCl[a] ≤50 mL/min)

Estimated CrCl[a] (mL/min)	cIAI/cUTI, Including Pyelonephritis	HABP/VABP
30 to 50	750 mg (500 mg and 250 mg) intravenously every 8 hours	1.5 g (1 g and 0.5 g) intravenously every 8 hours
15 to 29	375 mg (250 mg and 125 mg) intravenously every 8 hours	750 mg (500 mg and 250 mg) intravenously every 8 hours
ESRD on hemodialysis	A single loading dose of 750 mg (500 mg and 250 mg) followed by a 150 mg (100 mg and 50 mg) maintenance dose administered intravenously every 8 hours for the remainder of the treatment period (on hemodialysis days, administer the dose at the earliest possible time following completion of dialysis)	A single loading dose of 2.25 g (1.5 g and 0.75 g) followed by a 450 mg (300 mg and 150 mg) maintenance dose administered intravenously every 8 hours for the remainder of the treatment period (on hemodialysis days, administer the dose at the earliest possible time following completion of dialysis)

Dosage of ZERBAXA by infection in pediatric patients (birth to less than 18 years of age) with eGFR[c] greater than 50 mL/min/1.73 m²

Infection	Dose	Frequency	Infusion Time	Duration
Complicated Intra-abdominal Infections[b]	30 mg/kg up to a maximum dose of 1.5 g[d]	Every 8 hours	**1 hour**	5 to 14 days
Complicated Urinary Tract Infections including Pyelonephritis	30 mg/kg up to a maximum dose of 1.5 g[d]	Every 8 hours	**1 hour**	7 to 14 days

There is insufficient information to recommend a dosage regimen for pediatric patients with HABP/VABP.

[a]CrCl estimated using Cockcroft-Gault formula; [b]Used in conjunction with metronidazole 500 mg intravenously every 8 hours; [c]Estimated GFR using an age-appropriate equation for use in the pediatric population; [d]Pediatric patients weighing greater than 50 kg should not exceed a maximum dose of 1.5 g.

Dosage adjustments in pediatric patients with cUTI or cIAI and with renal impairment

Dosage adjustment of ZERBAXA in pediatric patients (birth to less than 18 years of age) with eGFR of 50 mL/min/1.73 m² or less has not been determined. ZERBAXA is not recommended in pediatric patients who have an eGFR 50 mL/min/1.73 m² or less.

cIAI, complicated intra-abdominal infection; CrCl, creatinine clearance; cUTI, complicated urinary tract infection; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HABP, hospital-acquired bacterial pneumonia; VABP, ventilator-associated bacterial pneumonia.

See Prescribing Information for detailed dosing and administration.

Important Safety Information for ZERBAXA *(continued)*

- **Pediatric Use:** There is insufficient information to recommend dosage adjustment for pediatric patients younger than 18 years of age with cIAI and cUTI with eGFR 50 mL/min/1.73m² or less. ZERBAXA is not recommended in pediatric patients who have an eGFR 50 mL/min/1.73m² or less. Pediatric patients born at term or pre-term may not have an eGFR of 50 mL/min/1.73m² or greater at birth or within the first few months of life.

Before prescribing ZERBAXA, please read the Prescribing Information.

References:
1. Data available on request from Merck Professional Services-DAP, WP1-27, PO Box 4, West Point, PA 19486-0004. Please specify information package US-ZER-01606. **2.** Norris AH, Shrestha NK, Allison GM, et al. 2018 Infectious Diseases Society of America clinical practice guideline for the management of outpatient parenteral antimicrobial therapy. *Clin Infect Dis.* 2019;68(1):e1-e35.doi:10.1093/cid/ciy745