Indications

ZERBAXA is indicated in adult patients for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis, caused by the following Gram-negative microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa*.

ZERBAXA used in combination with metronidazole is indicated in adult patients for the treatment of complicated intra-abdominal infections (cIAI) caused by the following 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 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.

Before prescribing ZERBAXA, please read the accompanying Prescribing Information.
Recommended Dosing Regimen for cUTI and cIAI Patients

The recommended dosage regimen of ZERBAXA® (ceftolozane and tazobactam) is 1.5 g (ceftolozane 1 g and tazobactam 0.5 g) for injection administered every 8 hours by IV infusion over 1 hour in patients 18 years or older.

Dosage of ZERBAXA 1.5 g (ceftolozane 1 g and tazobactam 0.5 g) by infection in patients with CrCl greater than 50 mL/min

<table>
<thead>
<tr>
<th>Infection</th>
<th>Dose</th>
<th>Frequency</th>
<th>Infusion time</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated Urinary Tract Infections, including Pyelonephritis</td>
<td>1.5 g</td>
<td>Every 8 hours</td>
<td>1 hour</td>
<td>7 days</td>
</tr>
<tr>
<td>Complicated Intra-Abdominal Infections*</td>
<td>1.5 g</td>
<td>Every 8 hours</td>
<td>1 hour</td>
<td>4 to 14 days</td>
</tr>
</tbody>
</table>

*Used in conjunction with metronidazole 500 mg intravenously every 8 hours.

The duration of therapy should be guided by the severity and site of infection and the patient’s clinical and bacteriological progress.

Important Safety Information

- **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, 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. 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 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.

Dosage in Patients With Impaired Renal Function

Because ZERBAXA is eliminated primarily by the kidneys, a dosage adjustment is required for patients whose CrCl is 50 mL/min or less, as shown below:

- The standard dose may be used in most patients with no dosage adjustments needed for age, gender, race, or hepatic impairment.
- For patients with changing renal function, monitor CrCl at least daily and adjust the dosage of ZERBAXA accordingly.

Dosage of ZERBAXA in patients with renal impairment

<table>
<thead>
<tr>
<th>Estimated CrCl (mL/min)*</th>
<th>Recommended dosage regimen for ZERBAXA 1.5 g (ceftolozane 1 g and tazobactam 0.5 g)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 to 50</td>
<td>750 mg (500 mg and 250 mg) intravenously every 8 hours</td>
</tr>
<tr>
<td>15 to 29</td>
<td>375 mg (250 mg and 125 mg) intravenously every 8 hours</td>
</tr>
<tr>
<td>End-stage renal disease on hemodialysis</td>
<td>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 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)</td>
</tr>
</tbody>
</table>

*CrCl estimated using Cockcroft-Gault formula.

Important Safety Information

- **Clostridium 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.

- **Development of drug-resistant bacteria:** Prescribing ZERBAXA in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

- **Adverse reactions:** The most common adverse reactions occurring in ≥5% of patients were headache (5.8%) in the cUTI trial, and nausea (7.9%), diarrhea (6.2%), and pyrexia (5.6%) in the cIAI trial.

Before prescribing ZERBAXA, please read the accompanying Prescribing Information.
A POWERFUL CHOICE
For patients with cUTIs and, in combination with metronidazole, cIAIs caused by designated pathogens.

Important Safety Information

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CrCl=creatinine clearance.

Before prescribing ZERBAXA, please read the accompanying Prescribing Information.

For additional copies of the Prescribing Information, please call 800-672-6372, visit zerbaxa.com, or contact your Merck representative.