ZERBAXA®
ceftolozane and tazobactam
for injection

Merck's Portfolio gives you...

The Power of Choice

Before prescribing ZERBAXA or RECARBRIO, please read the Prescribing Information for each product.

RECARBRIO™
(imipenem, cilastatin, and relebactam) for injection 1.25 g

ZERBAXA®
ceftolozane and tazobactam
for injection

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.

Additional Important Safety Information for ZERBAXA can be found on pages 3-5.

ASPECT-NP was unique among HABP/VABP registration trials

100% of the patients were ventilated

Selected baseline characteristics

Hospitalized for ≥5 days
- 77% of patients had been hospitalized for ≥5 days[1]

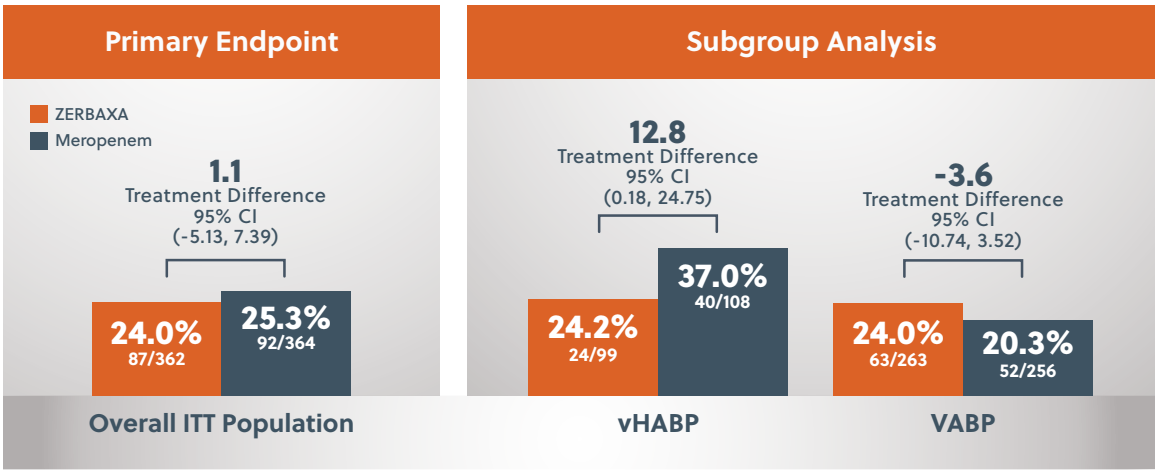
ASPECT-NP is unique among registration trials for nosocomial pneumonia
- 100% patients were intubated and mechanically ventilated
- 92% were treated in the ICU

Current antibiotic failure
- Approximately 13% of patients were failing current antibacterial therapy for HABP/VABP

Increased risk of mortality
- Median baseline APACHE score of 17, indicating a **24% mortality rate**[1]
- 1/3 of patients had an APACHE score of ≥20, indicating a **40% mortality rate**[2]

ZERBAXA fights HABP/VABP

ZERBAXA achieved primary endpoint of noninferiority to meropenem in day 28 all-cause mortality in the overall ITT population



Subgroup analysis: ZERBAXA showed a favorable response in day 28 all-cause mortality in the vHABP subgroup: ZERBAXA 24.2% vs meropenem 37.0%. In the VABP subgroup, day 28 all-cause mortality was 24.0% for ZERBAXA vs 20.3% for meropenem.

The analysis population for the primary endpoint was the ITT population, which included all randomized patients. The primary efficacy endpoint was all-cause mortality at day 28. The objective was to demonstrate the noninferiority of ZERBAXA versus meropenem in adults with VNP. For analysis of the treatment differences, 95% confidence intervals (CIs) were calculated as stratified Newcombe CIs.[1]

ASPECT-NP study design: Adult hospitalized patients with HABP/VABP (n=726) were randomly assigned (1:1) to receive ZERBAXA 3 g IV (n=362) over a 1-hour period every 8 hours or meropenem 1 g IV (n=364) every 8 hours for 8 to 14 days. Patients were stratified by vHABP/VABP diagnosis and by age (≥65 years and <65 years) and were assessed 7 to 14 days after the end of treatment and again at day 28. Primary endpoint was all-cause mortality at day 28. Objective was to demonstrate the noninferiority of ZERBAXA versus meropenem in adults with ventilated pneumonia.[1]

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.

Additional Important Safety Information for ZERBAXA can be found on pages 2, 4-5.

ZERBAXA®
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for injection

ZERBAXA demonstrated *in vitro* activity in the presence of certain mechanisms of resistance

P. aeruginosa isolates			ESBLs			
Chromosomal AmpC	Loss of outer membrane porin[a]	Upregulation of efflux pumps[b]	TEM	SHV	CTX-M	OXA
✓	✓	✓	✓	✓	✓	✓

[a]OprD, [b]MexXY, MexAB

- **ZERBAXA is not active against bacteria that produce serine carbapenemases [KPC] (*K. pneumoniae* carbapenemase) and metallo-beta-lactamases (MBLs)**

The clinical significance of *in vitro* data is unknown.

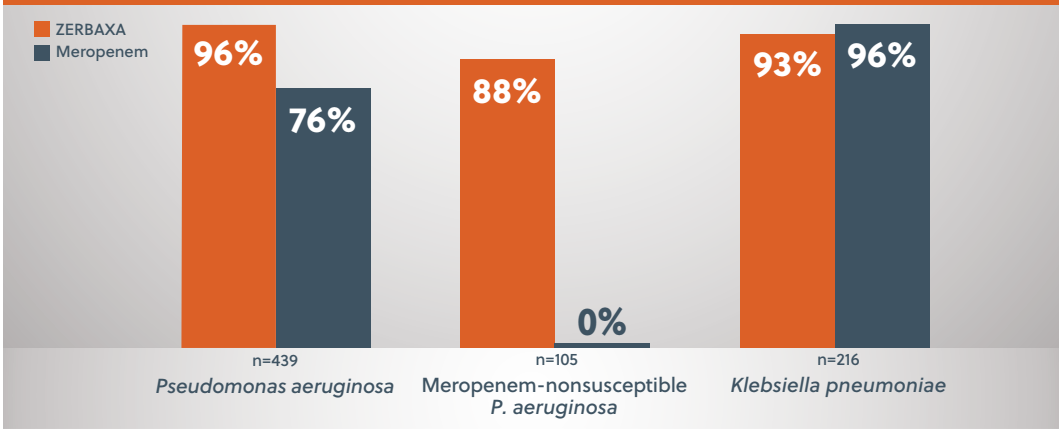
Important Safety Information for ZERBAXA *(continued)*

- **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%).
- **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/1.73m^2 or less. ZERBAXA is not recommended in pediatric patients who have an eGFR 50 mL/min/1.73m^2 or less. Pediatric patients born at term or pre-term may not have an eGFR of 50 mL/min/1.73m^2 or greater at birth or within the first few months of life.

Additional Important Safety Information for ZERBAXA can be found on pages 2-3, 5.

ZERBAXA demonstrated potent *in vitro* activity[3]

Susceptibility rates for select ICU respiratory tract isolates in surveillance data (2019-2020)[3,a]



- Culture and susceptibility information and local epidemiology should be considered in modifying antibacterial therapy

[a]Isolates were collected as part of the Study for Monitoring Antimicrobial Resistance Trends (SMART 2019-2020).[3]

The clinical significance of *in vitro* data is unknown.

SMART study design: The Study for Monitoring Antimicrobial Resistance Trends (SMART) was initiated by Merck in 2002 to monitor the *in vitro* susceptibility of clinical bacterial Gram-negative isolates to various antimicrobials in intra-abdominal, respiratory, and urinary tract infections. Collection of isolates from respiratory tract infections (RTI) started in 2015. This collection of RTI isolates started in 2019 and was completed in 2020. Minimum inhibitory concentration (MIC) values for ceftolozane/tazobactam and comparator agents were determined using the broth microdilution methodology recommended by the Clinical and Laboratory Standards Institute (CLSI) that was current in the year the data was collected. The following breakpoints were used to test for the susceptibility of *P. aeruginosa* (MICs [mcg/mL]): ≤4/4 (susceptible) for ZERBAXA and ≤2/4 (susceptible) for meropenem, and of *K. pneumoniae*: ≤2/4 (susceptible) for ZERBAXA and ≤1/4 (susceptible) for meropenem. Limitations of the SMART data include a lack of clinical information to confirm isolates being nosocomial versus community-acquired and the number of SMART investigator sites varied each year.[3]

Important Safety Information for ZERBAXA (*continued*)

- **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.

Before prescribing ZERBAXA, please read the additional Important Safety Information for ZERBAXA on pages 2-4, and the Prescribing Information.

RECARBRIO™ (imipenem, cilastatin, and relebactam) for injection 1.25 g

Indications for RECARBRIO

RECARBRIO is indicated for the treatment of patients 18 years of age and older with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP), caused by the following susceptible gram-negative microorganisms: *Acinetobacter calcoaceticus-baumannii complex, Enterobacter cloacae, Escherichia coli, Haemophilus influenzae, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Serratia marcescens.*

RECARBRIO is indicated in patients 18 years of age and older who have limited or no alternative treatment options, for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis, caused by the following susceptible gram-negative microorganisms: *Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa.*

RECARBRIO is indicated in patients 18 years of age and older who have limited or no alternative treatment options for the treatment of complicated intra-abdominal infections (cIAI) caused by the following susceptible gram-negative microorganisms: *Bacteroides caccae, Bacteroides fragilis, Bacteroides ovatus, Bacteroides stercoris, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Fusobacterium nucleatum, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Parabacteroides distasonis,* and *Pseudomonas aeruginosa.*

Approval of the cUTI and cIAI indications is based on limited clinical safety and efficacy data for RECARBRIO.

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of RECARBRIO and other antibacterial drugs, RECARBRIO 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.

Selected Safety Information for RECARBRIO

- **Hypersensitivity Reactions:** RECARBRIO is contraindicated in patients with a history of known severe hypersensitivity (severe systemic allergic reaction such as anaphylaxis) to any component of RECARBRIO. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving therapy with beta-lactams. Before initiating therapy with RECARBRIO, careful inquiry should be made concerning previous hypersensitivity reactions to carbapenems, penicillins, cephalosporins, other beta-lactams, and other allergens. If a hypersensitivity reaction to RECARBRIO occurs, discontinue the therapy immediately.
- **Seizures and Other Central Nervous System (CNS) Adverse Reactions:** CNS adverse reactions, such as seizures, confusional states, and myoclonic activity, have been reported during treatment with imipenem/cilastatin, a component of RECARBRIO, especially when recommended dosages of imipenem were exceeded. These have been reported most commonly in patients with CNS disorders (eg, brain lesions or history of seizures) and/or compromised renal function.

  Anticonvulsant therapy should be continued in patients with known seizure disorders. If CNS adverse reactions including seizures occur, patients should undergo a neurological evaluation to determine whether RECARBRIO should be discontinued.

Additional Selected Safety Information for RECARBRIO can be found on pages 7-9.

In a registration trial, RECARBRIO achieved the primary endpoint of noninferiority vs piperacillin/tazobactam in day 28 all-cause mortality in the MITT population[4,a]

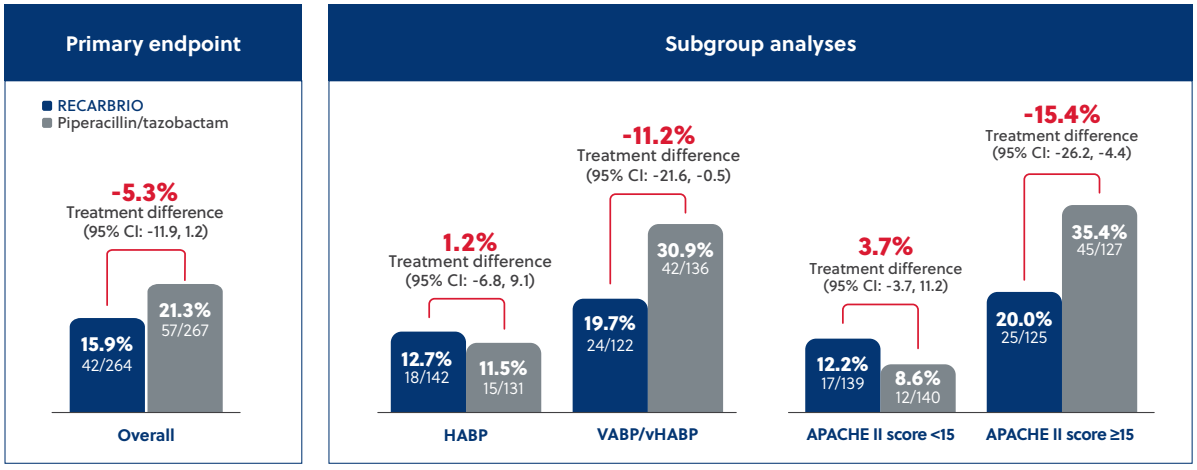
Selected baseline characteristics

Hospitalization
- 77% of patients had been hospitalized for ≥5 days
- 66% of patients were in the ICU

Ventilation
- 260 (49%) patients were ventilated at enrollment, including 194 (36%) patients with VABP and 66 (12%) patients with vHABP

Microbiology
- **22% had polymicrobial infection**
- 5.8% had concurrent bacteremia

Increased risk of mortality
- **Mean APACHE II score was 15** and **47% of patients** had an APACHE II score **≥15 at baseline**, indicating a 24% mortality rate[2]



[a]MITT population is defined as all randomized participants who received at least 1 dose of trial treatment and did not have only Gram-positive cocci on Gram stain of the baseline lower respiratory tract specimen. Noninferiority defined as: upper bound of the 2-sided 95% confidence interval (CI) for the adjusted treatment difference (IMI/REL minus PIP/TAZ) was <10 percentage points.[4]

RECARBRIO demonstrated a favorable response in certain high-risk subgroups

- VABP/vHABP patients
- Patients with APACHE II scores ≥15

Study design: 535 hospitalized adults with HABP/VABP were randomized and received either RECARBRIO 1.25 g or piperacillin/tazobactam 4.5 g IV over a 30-minute period every 6 hours for 7 to 14 days of therapy. Eligible patients were stratified by nonventilated HABP vs ventilated HABP/VABP and by Acute Physiology and Chronic Health Evaluation II ([APACHE II] score <15 vs ≥15). Primary efficacy endpoint was all-cause mortality at day 28 in the MITT population.[4]

Selected Safety Information for RECARBRIO *(continued)*

- **Increased Seizure Potential Due to Interaction with Valproic Acid:** Concomitant use of RECARBRIO, with valproic acid or divalproex sodium may increase the risk of breakthrough seizures. Avoid concomitant use of RECARBRIO with valproic acid or divalproex sodium or consider alternative antibacterial drugs other than carbapenems.

Additional Selected Safety Information for RECARBRIO can be found on pages 6, 8-9.

RECARBRIO™ (imipenem, cilastatin, and relebactam) for injection 1.25 g

RECARBRIO is active *in vitro* against key pathogens with certain mechanisms of resistance

P. aeruginosa			Enterobacteriaceae		
Upregulation of AMP-C or PDC	Loss of outer membrane porin[a]	Upregulation of efflux pumps[b]	Certain ESBLs	Some KPCs	ACT/MIR (An AMP-C)
✓	✓	✓	✓	✓	✓

[a]OprD, [b]MexAB, MexCD, MexJK, MexXY

- **RECARBRIO is not active against most isolates containing MBLs, some oxacillinases with carbapenemase activity, as well as certain alleles of GES**

The clinical significance of *in vitro* data is unknown.

Selected Safety Information for RECARBRIO *(continued)*

- ***Clostridioides difficile*–Associated Diarrhea (CDAD)** has been reported with use of nearly all antibacterial agents, including RECARBRIO, and may range in severity from mild diarrhea to fatal colitis. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against *C difficile* may need to be discontinued.
- **Development of Drug-Resistant Bacteria:** Prescribing RECARBRIO in the absence of a proven or strongly suspected bacterial infection or prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
- **Adverse Reactions:** The most frequently reported adverse reactions occurring in ≥5% of HABP/VABP patients treated with RECARBRIO were aspartate aminotransferase increased (11.7%), anemia (10.5%), alanine aminotransferase increased (9.8%), diarrhea (7.9%), hypokalemia (7.9%), and hyponatremia (6.4%). The most frequently reported adverse reactions occurring in ≥2% of cUTI and cIAI patients treated with RECARBRIO were diarrhea (6%), nausea (6%), headache (4%), vomiting (3%), alanine aminotransferase increased (3%), aspartate aminotransferase increased (3%), phlebitis/infusion site reactions (2%), pyrexia (2%), and hypertension (2%).

Additional Selected Safety Information for RECARBRIO can be found on pages 6-7, 9.

RECARBRIO demonstrated potent *in vitro* activity[5]

In vitro susceptibility		
	Imipenem/relebactam	**Piperacillin/tazobactam**
***P. aeruginosa*[a]**		
P. aeruginosa (n=1641)	**90%**	79%
Pip/tazo NS *P. aeruginosa* (n=345)	**71%**	0%
Enterobacteriaceae[a,b]		
Enterobacteriaceae (n=6339)	**99%**	91%
Pip/tazo NS Enterobacteriaceae (n=584)	**97%**	0%
E. coli (n=2769)	**100%**	96%
Pip/tazo NS *E. coli* (n=126)	**100%**	0%
K. pneumoniae (n=1268)	**99%**	92%
Pip/tazo NS *K. pneumoniae* (n=108)	**94%**	0%
***K. pneumoniae* (2016-2020)[a]**		
K. pneumoniae (n=3333)	**99%**	90%
KPC+ *K. pneumoniae* (n=76)	**93%**	0%
ESBL+ Enterobacteriaceae[a,b]		
ESBL+ Enterobacteriaceae (n=1244)	**98%**	67%
ESBL+ *E. coli* (n=585)	**100%**	86%
ESBL+ *K. pneumoniae* (n=233)	**97%**	64%

[a]Isolates collected from urinary, intra-abdominal, lower respiratory tract, and bloodstream infection samples from both ICU and non-ICU settings in the United States from 2016-2020 for *K. pneumoniae* (including KPC+) and 2019-2020 for other listed isolates for the SMART surveillance program.[5]

[b]Enterobacteriaceae: *C. freundii, E. cloacae, E. coli, K. aerogenes, K. oxytoca, K. pneumoniae, S. marcescens.*[5]

- **Culture and susceptibility information and local epidemiology should be considered in modifying antibacterial therapy[5]**

The clinical significance of *in vitro* data is unknown.

SMART study design: The Study for Monitoring Antimicrobial Resistance Trends (SMART) was initiated by Merck in 2002 to monitor the *in vitro* susceptibility of clinical bacterial Gram-negative isolates to various antimicrobials in intra-abdominal, respiratory, urinary tract infections, and bloodstream infections. Collection of isolates from respiratory tract infections (RTI) started in 2015. Minimum inhibitory concentration (MIC) values for imipenem/relebactam and comparator agents were determined using the broth microdilution methodology recommended by the Clinical and Laboratory Standards Institute (CLSI) that was current in the year the data was collected. The following breakpoints were used to test for the susceptibility of *P. aeruginosa* (MICs [mcg/mL]): ≤2/4 (susceptible) for RECARBRIO and ≤16/4 (susceptible) for piperacillin/tazobactam, and of Enterobacteriaceae: ≤1/4 (susceptible) for RECARBRIO and ≤16/4 (susceptible) for piperacillin/tazobactam. Limitations of the SMART data include a lack of clinical information to confirm isolates being nosocomial versus community-acquired and the number of SMART investigator sites varied each year.[5,6]

Selected Safety Information for RECARBRIO *(continued)*

- **Hypersensitivity Reactions:** RECARBRIO is contraindicated in patients with a history of known severe hypersensitivity (severe systemic allergic reaction such as anaphylaxis) to any component of RECARBRIO. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving therapy with beta-lactams. Before initiating therapy with RECARBRIO, careful inquiry should be made concerning previous hypersensitivity reactions to carbapenems, penicillins, cephalosporins, other beta-lactams, and other allergens. If a hypersensitivity reaction to RECARBRIO occurs, discontinue the therapy immediately.

Before prescribing RECARBRIO, please read the additional Selected Safety Information for RECARBRIO on pages 6-8, and the Prescribing Information.

Learn More

The **Merck antibiotic portfolio**, ZERBAXA and RECARBRIO, gives you the **Power of Choice** for the treatment of your appropriate patients with HABP/VABP, cUTI, or cIAI

ZERBAXA® ceftolozane and tazobactam for injection

Consider ZERBAXA: For suspected or confirmed *P. aeruginosa* in appropriate critically ill patients with **HABP/VABP** who are continuing to decline[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.

Before prescribing ZERBAXA, please read the additional Important Safety Information for ZERBAXA on pages 2-5, and the Prescribing Information.

RECARBRIO™ (imipenem, cilastatin, and relebactam) for injection 1.25 g

Consider RECARBRIO's broad coverage: For appropriate patients with cUTI, cIAI, or HABP/VABP caused by some of the most common Gram-negative pathogens

Indications for RECARBRIO

RECARBRIO is indicated for the treatment of patients 18 years of age and older with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP), caused by the following susceptible gram-negative microorganisms: *Acinetobacter calcoaceticus-baumannii complex, Enterobacter cloacae, Escherichia coli, Haemophilus influenzae, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Serratia marcescens.*

RECARBRIO is indicated in patients 18 years of age and older who have limited or no alternative treatment options, for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis, caused by the following susceptible gram-negative microorganisms: *Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa.*

RECARBRIO is indicated in patients 18 years of age and older who have limited or no alternative treatment options for the treatment of complicated intra-abdominal infections (cIAI) caused by the following susceptible gram-negative microorganisms: *Bacteroides caccae, Bacteroides fragilis, Bacteroides ovatus, Bacteroides stercoris, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Fusobacterium nucleatum, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Parabacteroides distasonis,* and *Pseudomonas aeruginosa.*

Approval of the cUTI and cIAI indications is based on limited clinical safety and efficacy data for RECARBRIO.

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of RECARBRIO and other antibacterial drugs, RECARBRIO 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.

Selected Safety Information for RECARBRIO

- **Hypersensitivity Reactions:** RECARBRIO is contraindicated in patients with a history of known severe hypersensitivity (severe systemic allergic reaction such as anaphylaxis) to any component of RECARBRIO. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving therapy with beta-lactams. Before initiating therapy with RECARBRIO, careful inquiry should be made concerning previous hypersensitivity reactions to carbapenems, penicillins, cephalosporins, other beta-lactams, and other allergens. If a hypersensitivity reaction to RECARBRIO occurs, discontinue the therapy immediately.

Before prescribing RECARBRIO, please read the additional Selected Safety Information for RECARBRIO on pages 6-9, and the Prescribing Information.

References:

1. Kollef MH, Nováček M, Kivistik Ü, et al. Ceftolozane-tazobactam versus meropenem for treatment of nosocomial pneumonia (ASPECT-NP): a randomised, controlled, double-blind, phase 3, non-inferiority trial. *Lancet Infect Dis.* 2019;19(12):1299-1311. doi:10.1016/S1473-3099(19)30403-7 **2.** Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med.* 1985;13(10):818-829. **3.** Data available on request from Merck & Co., Inc., Professional Services DAP, WPI-27, PO Box 4, West Point, PA 19486-0004. Please specify information package US-ZER-01502. **4.** Titov I, Wunderink RG, Roquilly A, et al. A randomized, double-blind, multicenter trial comparing efficacy and safety of imipenem/cilastatin/relebactam versus piperacillin/tazobactam in adults with hospital-acquired or ventilator-associated bacterial pneumonia (RESTORE-IMI 2 Study). *Clin Infect Dis.* 2021;73(11):e4539-e4548. doi:10.1093/cid/ciaa803 **5.** Data available on request from Merck & Co., Inc., Professional Services DAP, WPI-27, PO Box 4, West Point, PA 19486-0004. Please specify information package US-TIX-00522. **6.** CLSI. *Performance Standards for Antimicrobial Susceptibility Testing.* 31st ed. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2021.

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