The first and only treatment targeting HABP/VABP caused by susceptible isolates, which can include multidrug-resistant strains of *Acinetobacter baumannii-calcoaceticus* complex[1,2]

INDICATION & USAGE

Indication

XACDURO® (sulbactam for injection; durlobactam for injection), co-packaged for intravenous use is indicated in adults for the treatment of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) caused by susceptible isolates of *Acinetobacter baumannii-calcoaceticus* complex.

Limitations of Use

XACDURO is not indicated for the treatment of HABP/VABP caused by pathogens other than susceptible isolates of *Acinetobacter baumannii-calcoaceticus* complex.

Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of XACDURO and other antibacterial drugs, XACDURO should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

SELECTED IMPORTANT SAFETY INFORMATION

Contraindications: XACDURO is contraindicated in patients with a history of known severe hypersensitivity to the components of XACDURO or other beta-lactam antibacterial drugs.

Please see additional Important Safety Information throughout. Before administering, please see the accompanying Full Prescribing Information for XACDURO.

ACINETOBACTER SHOULD BE STOPPED

Rates of incidence are on the rise[3]

5th most common cause of deaths attributable to drug resistance across the globe[4]

Can be deadly, with a 26.0% to 55.7% mortality rate[5]

Poses a threat to patients on ventilators in hospitals and nursing homes[6]

***Acinetobacter* has become resistant to most antibiotics used to treat HABP/VABP, including carbapenems and third-generation cephalosporins[6]**

Carbapenem-resistant *Acinetobacter* is classified as a critical priority pathogen by the World Health Organization[6]

The spread is alarming, with a 78% increase in carbapenem-resistant *Acinetobacter baumannii* (CRAB) cases in US hospitals in 2020.[3]

Outcomes are worse in patients with CRAB infections:*

- 2 days longer hospital stay on average[7]
- 17.2% higher rate of ICU utilization[7]
- 2x higher chance of in-hospital death[8]

*In comparison to patients with carbapenem-susceptible *Acinetobacter baumannii*

***Acinetobacter* has become increasingly difficult to treat and there is no clear standard-of-care antibiotic regimen for CRAB infections.[9]**

ATTACK & RESTORE

XACDURO combines sulbactam with novel durlobactam creating a powerful duo against *Acinetobacter* infections

Sulbactam attacks Acinetobacter

- Penicillin derivative with intrinsic activity against *Acinetobacter*
- Clinical utilization may be limited because β-lactam resistance is common[10]

Durlobactam restores sulbactam

- Diazabicyclooctane β-lactamase inhibitor
- Potent inhibitor of class A, C, and D β-lactamases
- Restores sulbactam activity *in vitro* and *in vivo*

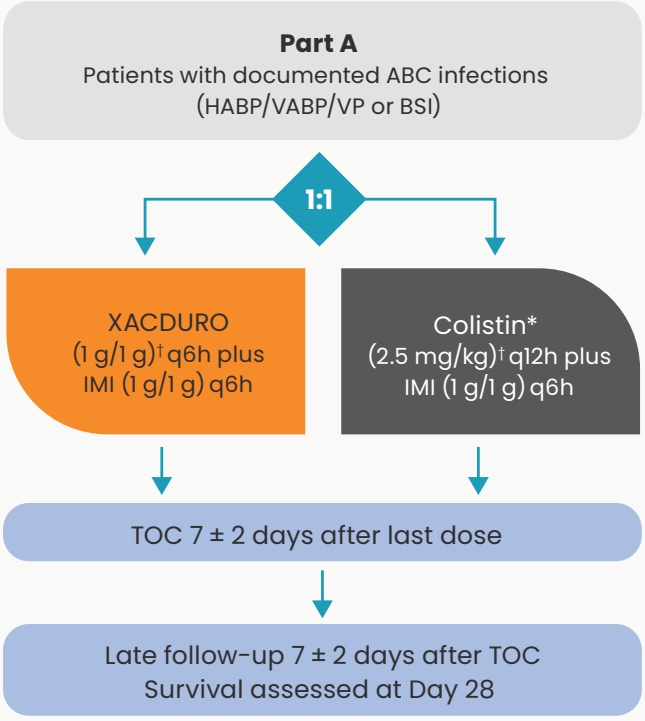
SELECTED IMPORTANT SAFETY INFORMATION

Warnings and Precautions:

- Hypersensitivity was observed in patients treated with XACDURO in clinical trials. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions and serious skin reactions have been reported in patients receiving beta-lactam antibacterial drugs. Before initiating therapy with XACDURO, careful inquiry should be made concerning previous hypersensitivity reactions to carbapenems, penicillins, cephalosporins, other beta lactams, and other allergens. If an allergic reaction occurs, discontinue XACDURO.

A LANDMARK TRIAL

ATTACK is a Phase 3, multinational, randomized, controlled, noninferiority trial conducted to evaluate the efficacy and safety of XACDURO versus colistin* for patients with serious infections due to ABC, including CRABC strains.[2]



***Both in combination with imipenem/cilastatin as background therapy.**

†XACDURO dosing was adjusted for renal function. Colistin dosing was adjusted to ideal body weight and renal function. A single colistin loading dose of 2.5 to 5 mg/kg given intravenously over 3 to 6 minutes (or according to standard-of-care) was administered on Day 1 for patients who had not received prior colistin therapy.

ABC=*Acinetobacter baumannii-calcoaceticus* complex; ATTACK=*Acinetobacter* Treatment Trial Against Colistin; BSI=bloodstream infection; CRABC=carbapenem-resistant *Acinetobacter baumnnii-calcoaceticus* complex; IMI=imipenem/cilastatin; qxh=every x hours; TOC=test of cure; VP=ventilated pneumonia.

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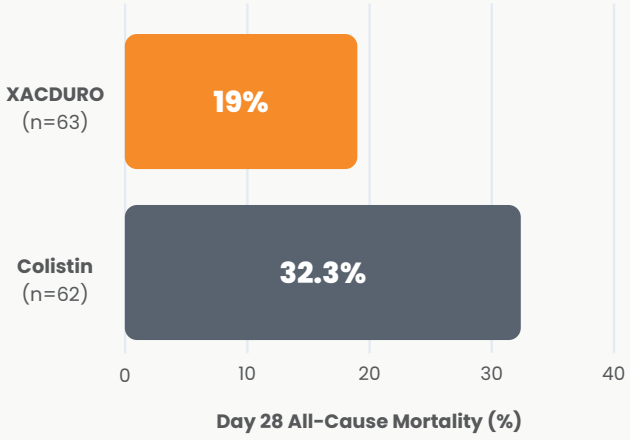
XACDURO® (sulbactam for injection; durlobactam for injection), co-packaged for intravenous use

POWERFUL RESULTS IN HABP/VABP CAUSED BY *ACINETOBACTER*

XACDURO MEANINGFULLY LOWERED ALL-CAUSE MORTALITY[2]



Reduced patient mortality and improved survival[2]

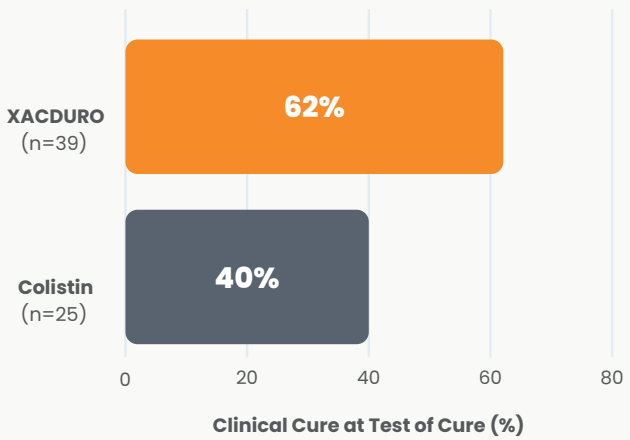
Primary efficacy endpoint:
28-day all-cause mortality in patients with laboratory-confirmed CRABC (microbiologically modified intent to treat population).

When treating HABP/VABP caused by *Acinetobacter*, act fast with XACDURO

SELECTED IMPORTANT SAFETY INFORMATION
Warnings and Precautions (cont'd):

- *Clostridioides difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents and may range in severity from mild diarrhea to fatal colitis. Evaluate if diarrhea occurs. If CDAD is suspected or confirmed, the risk/benefit of continuing treatment with XACDURO should be assessed.

XACDURO ACHIEVED SIGNIFICANTLY GREATER CLINICAL CURE RATES VERSUS COLISTIN[2]



62% cure rate at test of cure[2]

Prespecified secondary efficacy endpoint:
Clinical cure at the TOC (7 ± 2 days after end of therapy) visit in all populations.

Scan the QR code to read more about the XACDURO phase 3 clinical trial in *The Lancet ID*.

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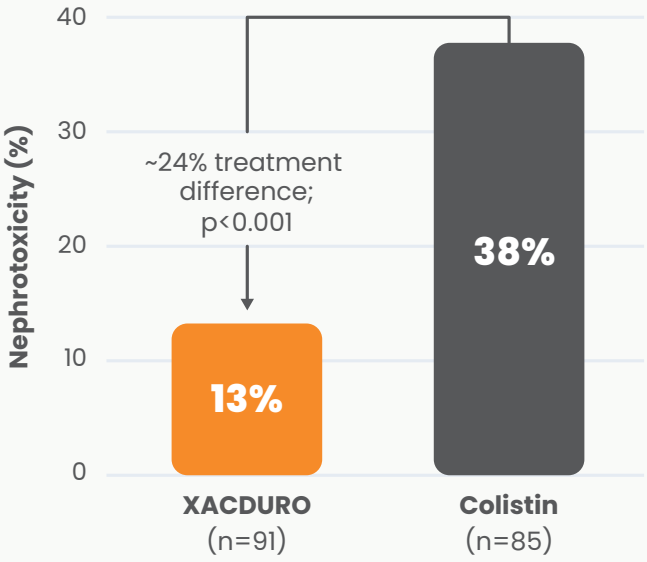
SIGNIFICANTLY REDUCED NEPHROTOXICITY VS. COLISTIN

INCIDENCE OF NEPHROTOXICITY AS MEASURED BY THE RIFLE CRITERIA* AT ANY POST-BASELINE VISIT[2]



For patients with creatinine clearance <45 mL/min and ≥130 mL/min, please see the accompanying Full Prescribing Information.

*RIFLE (risk, injury, failure, loss, or end-stage renal disease) measured by creatinine level or glomerular filtration rate, but not urinary output. Nephrotoxicity defined as meeting any of the RIFLE criteria at any post-baseline visit; if patients had multiple RIFLE events, the patient was counted only once at the highest severity. No patients in this study experienced end-stage renal disease.

SELECTED IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd):

- Prescribing XACDURO in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

SELECTED ADVERSE REACTIONS (>5% FREQUENCY)

Adverse Reaction	XACDURO (N=91) n (%)	Colistin (N=86) n (%)
Any adverse reaction	80 (88)	81 (94)
Liver test abnormalities†	17 (19)	18 (21)
Diarrhea	15 (17)	9 (11)
Anemia	12 (13)	12 (14)
Hypokalemia	11 (12)	9 (11)
Arrhythmia	8 (9)	8 (9)
Acute kidney injury†	5 (6)	31 (36)
Thrombocytopenia	5 (6)	3 (4)
Constipation	5 (6)	5 (6)

†Liver test abnormalities includes the following adverse reactions: liver function test abnormal, hepatic function abnormal, increased transaminases, ALT increased, and AST increased; Acute kidney injury includes the following adverse reactions: renal impairment, blood Cr increased, toxic nephropathy, renal failure and acute kidney injury.

Adverse reactions leading to discontinuation of treatment occurred in 11% of XACDURO patients vs. 16% of colistin patients. One patient treated with XACDURO developed anaphylactic shock which led to discontinuation of treatment.

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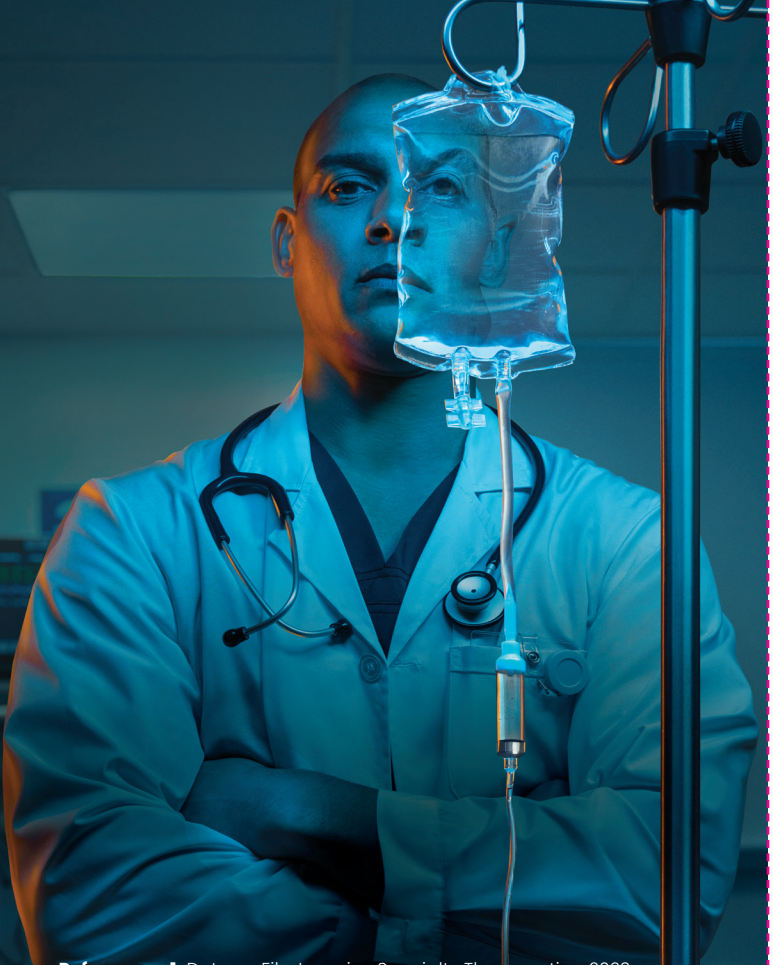
XACDURO® (sulbactam for injection; durlobactam for injection), co-packaged for intravenous use



References: 1. Data on File. Innoviva Specialty Therapeutics; 2023. **2.** Kaye KS, Shorr AF, Wunderink RG, et al. Efficacy and safety of sulbactam-durlobactam versus colistin for the treatment of patients with serious infections caused by *Acinetobacter baumannii-calcoaceticus* complex: a multicentre, randomised, active-controlled, phase 3, non-inferiority clinical trial (ATTACK). *Lancet Infect Dis*. Published online May 11, 2023. doi:10.1016/S1473-3099(23)00184-6. **3.** CDC. COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2022. **4.** Murray CJL, Ikuta KS, Sharara F, et al. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet*. 2022; 399(10325):629-655. **5.** Appaneal HJ, Lopes VV, LaPlante KL, Caffrey AR. Treatment, Clinical Outcomes, and Predictors of Mortality among a National Cohort of Admitted Patients with *Acinetobacter baumannii* Infection. *Antimicrobial Agents and Chemotherapy*. 2022;66(3):1-2. doi:10.1128/AAC.01975-21 **6.** WHO publishes list of bacteria for which new antibiotics are urgently needed. World Health Organization. Published February 27, 2017. Accessed June 19, 2023. https://www.who.int/news/item/27-02-2017-who-publishes-list-ofbacteria-for-which-new-antibiotics-are-urgently-needed. **7.** Pogue JM, Zhou Y, Kanakamedala H, Cai B. Burden of illness in carbapenem-resistant *Acinetobacter baumannii* infections in US hospitals between 2014 and 2019. *BMC Infect Dis*. 2022;22:36. **8.** Lemos EV, de la Hoz FP, Einarson TR, et al. Carbapenem resistance and mortality in patients with *Acinetobacter baumannii* infection: systematic review and meta-analysis. *Clin Microbiol Infect*. 2014;20(5):416-423. **9.** Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. IDSA 2023 Guidance on the Treatment of Antimicrobial Resistant Gram-Negative Infections. *Infectious Diseases Society of America*. Published June 6, 2023. Accessed June 19, 2023. https://www.idsociety.org/practice-guideline/amr-guidance/ **10.** Pandey N, Cascella M. Beta-lactam antibiotics. *StatPearls*. Updated September 26, 2022. Accessed August 9, 2023. https://www.ncbi.nlm.nih.gov/books/NBK545311/

DOSING INFORMATION

Dose of XACDURO (g)
sulbactam 1 g and durlobactam 1 g

Frequency
Every 6 hours

- For more information on dosing and administration, see Full Prescribing Information
- Adjustments to the dosing regimen are recommended for patients with creatinine clearance (CLcr) <45 mL/min and for patients with augmented renal clearance (CLcr ≥130 mL/min). For patients undergoing intermittent hemodialysis (HD), start the dosing of XACDURO immediately after the completion of HD
- For patients with fluctuating renal function, monitor CLcr and adjust dosage accordingly
- **The recommended duration of treatment with XACDURO is 7 to 14 days. The duration of therapy should be guided by the patient's clinical status**

SELECTED IMPORTANT SAFETY INFORMATION

Adverse Reactions: The most common adverse reactions reported in >10% of patients treated with XACDURO were liver test abnormalities (19%), diarrhea (17%), anemia (13%), and hypokalemia (12%).

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XACDURO®
(sulbactam for injection; durlobactam for injection),
co-packaged for intravenous use

HABP/VABP KILLS QUICKLY, ACT FAST WITH XACDURO

Effective against *Acinetobacter* including drug-resistant strains such as CRAB[2]

Reduced patient mortality, improved survival and significantly greater cure rates vs. colistin[2]

Favorable safety profile with lower rates of nephrotoxicity vs. colistin[2]

Learn more about the first and only treatment targeting HABP/VABP caused by susceptible isolates, which can include multidrug-resistant strains of *Acinetobacter baumannii-calcoaceticus* complex[1,2] at XACDURO.com

SELECTED IMPORTANT SAFETY INFORMATION

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INNOVIVA Specialty Therapeutics

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