Effective Date: 10/25/2023
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Last P&T Approval/Version: 10/25/2023
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Policy Number: C26432-A

Xacduro (sulbactam/durlobactam)

PRODUCTS AFFECTED

Xacduro (sulbactam/durlobactam)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. HOSPITAL-ACQUIRED BACTERIAL PNEUMONIA/VENTILATOR-ASSOCIATED BACTERIAL PNEUMONIA (HABP/VABP):
   1. Documented diagnosis of hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia (HABP/VABP)
      AND

2. Documentation infection is causes by a susceptible isolate of Acinetobacter baumannii-calcoaceticus complex
   AND
3. Prescriber attests member had an inadequate treatment response, serious side effects, clinical contraindication, or non-susceptibility to other treatments (e.g., ampicillin/sulbactam, colistin, etc.)

CONTINUATION OF THERAPY:
N/A

DURATION OF APPROVAL:
Initial authorization: 14 days, Continuation of Therapy: N/A

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified infectious disease specialist [If prescribed in consultation, consultation notes must be submitted with initial request]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
1g/1g every 6 hours for 7-14 days

Maximum Quantity Limits – If CrCl is >140 mL/min (based on Cockcroft-Gault equation), give every 4 hours (See Appendix)

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for medical benefit coverage administered in a place of service that is an inpatient hospital or facility.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Beta-lactamase Inhibitor - Combination

FDA-APPROVED USES:
Indicated in patients 18 years of age and older 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.
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.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

Dosage of XACDURO (Sulbactam and Durlobactam) in Patients (18 Years of Age and Older) Based on Renal Function

Dose of Xacduro	Estimated CLcr (mL/min)*	Frequency
sulbactam 1g and durlobactam 1g	>/= 130	Every 4 hours
	45 to 129	Every 6 hours
	30 to 44	Every 8 hours
	15 to 29	Every 12 hours
	<15~	For patient initiating: Every 12 hours for the first 3 doses (0, 12, 24 hours), followed by every 24 hours after the third dose~ For patient currently receiving whose CLcr declines to <15: Every 24 hours

*CLcr = creatinine clearance estimated by Cockcroft-Gault equation
~ For patients on hemodialysis, the dose should be administered after the dialysis session has ended

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

A total of 177 hospitalized adults with documented Acinetobacter baumannii-calcoaceticus complex infections were randomized and treated in a multicenter, active-controlled, investigator unblinded, independent assessor-blinded, non-inferiority, phase 3 trial (Trial 1, NCT03894046). Patients were treated with either XACDURO (1 g sulbactam and 1 g durlobactam, or renally adjusted dose) intravenously over 3 hours every 6 hours (n = 91) or colistin 2.5 mg/kg (or renally adjusted dose) intravenously over 30 minutes every 12 hours after an initial loading dose of colistin 2.5 to 5 mg/kg (n = 86). Both treatment arms also received 1 g imipenem/1 g cilastatin (or renally adjusted dose) intravenously every 6 hours as background therapy for potential HABP/VABP pathogens other than Acinetobacter baumannii-calcoaceticus complex. Patients received up to 14 days of therapy. The primary efficacy endpoint for the study was 28-day all-cause mortality in the patients who received any amount of study medication with a confirmed baseline infection with carbapenem resistant Acinetobacter baumannii-calcoaceticus complex (CRABC microbiologically modified intent to treat (m-MITT) population). Among 128 patients in the CRABC m-MITT population, 125 patients who did not withdraw consent prior to assessment of survival status at Day 28 were assessed: 63 patients in the XACDURO group and 62 patients in the colistin group. For the primary endpoint of Day 28 all-cause mortality in the CRABC mMITT population, Xacduro was non-inferior to colistin with regard to Day 28 all-cause mortality.
Clinical cure rates were also evaluated. Clinical cure was defined as complete resolution or significant improvement of signs and symptoms that were present at baseline and no new symptoms, such that no additional gram-negative antimicrobial therapy was warranted. Clinical cure rates in the CRABC m-MITT population at the Test of Cure (TOC) Visit that was 7 days (±2 days) after the end of treatment were 39/63 (61.9%) for XACDURO versus 25/62 (40.3%) for colistin.

At the time of publication of the IDSA 2023 guidelines for treatment of antimicrobial resistant gram-negative infections, Xacduro was not yet FDA approved. Suggested approach to treatment per guidelines is high-dose ampicillin-sulbactam (total daily dose of 6-9 grams of the sulbactam component) in combination with at

least one other agent is suggested for the treatment of Carbapenem-resistant Acinetobacter baumannii (CRAB) infections. Also of note, the guidelines indicate “there is no clear “standard of care” antibiotic regimen for CRAB infections.”

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Xacduro (sulbactam/durlobactam) are considered experimental/investigational and therefore, will follow Molina’s Off- Label policy. Contraindications to Xacduro (sulbactam/durlobactam) include: known history of severe hypersensitivity to the components of Xacduro (sulbactam and durlobactam), or other beta-lactam antibacterial drugs.

OTHER SPECIAL CONSIDERATIONS:
Adjustments to the dosing regimen for XACDURO are recommended for patients with CLcr less than 45 mL/min and for patients with CLcr greater than or equal to 130 mL/min.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J3490	Unclassified drug (Xacduro)

AVAILABLE DOSAGE FORMS:
Xacduro SOLR 1-1GM

REFERENCES

1. Xacduro (sulbactam for injection; durlobactam for injection), co-packaged for intravenous use [prescribing information]. Waltham, MA: La Jolla Pharmaceutical Company; May 2023.
2. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Antimicrobial-Resistant Treatment Guidance: Gram-Negative Bacterial Infections. Infectious Diseases Society of America 2023; Version 3.0. Available at https://www.idsociety.org/practice-guideline/amr-guidance/. Accessed 6 October 2023.

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q4 2023