BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

NUZYRA™ (omadacycline) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for NUZYRA (omadacycline)

Criteria for Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with an Infectious Disease Specialist

Indication
- Community acquired bacterial pneumonia (CABP) caused by susceptible bacteria
- Acute bacterial skin and skin structure infection (ABSSSI) caused by susceptible bacteria

- Transition from intravenous therapy to oral therapy to facilitate hospital discharge

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Completed baseline culture and sensitivity report to identify microorganism and antimicrobial susceptibilities before starting treatment

Alternative Therapies (**Note:** Antibiotic selection varies based on the severity of illness, likelihood of infection with drug resistant pathogens, drug allergies or other factors)
- **For non hospitalized community acquired bacterial pneumonia (CABP) ONE** of the following:
  - Failure (trial for at least three months duration), contraindication, intolerance, or is not a candidate for:
    1. Beta lactam (e.g. high dose amoxicillin, amoxicillin clavulanate) plus either a macrolide (e.g., azithromycin, clarithromycin) or doxycycline
    2. Monotherapy with a respiratory fluoroquinolone (e.g., levofloxacin, moxifloxacin)
    3. Monotherapy with a macrolide (e.g., azithromycin, clarithromycin)
- **For hospitalized community acquired bacterial pneumonia (CABP) ONE** of the following:
  - Failure (trial for at least three months duration), contraindication, intolerance, or is not a candidate for:
    1. Anti pneumococcal beta lactam (e.g., ceftriaxone, cefotaxime, ceftaroline, ertapenem, ampicillin sulbactam) plus a macrolide (ex., azithromycin, clarithromycin) or doxycycline
    2. Monotherapy with a respiratory fluoroquinolone (e.g., levofloxacin, moxifloxacin)
- **For community acquired bacterial pneumonia (CABP) *with* methicillin resistant Staphylococcus aureus (MRSA) ONE** of the following:
  - Failure (trial for at least three months duration), contraindication, intolerance, or is not a candidate for:
    1. Linezolid
    2. Vancomycin
- **For acute bacterial skin and skin structure infection (ABSSSI) *without* MRSA ONE** of the following:
  - Failure (trial for at least three months duration), contraindication, intolerance, or is not a candidate for:
    1. Beta lactam (e.g., cephalexin, amoxicillin)
    2. Doxycycline
    3. Trimethoprim sulfamethoxazole
    4. Clindamycin
- **For acute bacterial skin and skin structure infection (ABSSSI) *with* MRSA, localized mild infection with no systemic symptoms ONE** of the following:
  - Failure (trial for at least three months duration), contraindication, intolerance, or is not a candidate for:
    1. Trimethoprim sulfamethoxazole
    2. Doxycycline
    3. Minocycline
- **For acute bacterial skin and skin structure infection (ABSSSI) *with* MRSA, extensive involvement, rapidly progressing with systemic symptoms or immune compromised ONE** of the following given intravenously then switch to oral when hemodynamically appropriate:
  - Failure (trial for at least three months duration), contraindication, intolerance, or is not a candidate for:

1. Linezolid
2. Tedizolid
3. Delafloxacin

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- No concomitant drug use with significant interacting drugs
- No known hypersensitivity to tetracycline class antibacterial drugs

Documentation Requirements

- A completed request form must be submitted including:
  - Chart notes
  - Lab results (culture and sensitivity report)
  - Supporting clinical documentation

Criteria Approval Duration

- 14 days total treatment (includes number of days of inpatient intravenous use) OR end of plan year
- IV infusion or injections – MEDICAL BENEFIT ONLY
- No refills will be authorized
- Any request for refill or continuation will be reviewed as a new request

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

Nuzyra (omadacycline) is a tetracycline class antibacterial indicated for the treatment of adult patients with infections caused by susceptible microorganisms seen in community acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infection (ABSSSI). Nuzyra (omadacycline) should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

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Omadacycline is an aminomethylcycline antibacterial within the tetracycline class of antibacterial drugs. Omadacycline binds to the 30S ribosomal subunit and blocks protein synthesis. Omadacycline is active *in vitro* against Gram-positive bacteria expressing tetracycline resistance active efflux pumps and ribosomal protection proteins. In general, omadacycline is considered bacteriostatic; however, omadacycline has demonstrated bactericidal activity against some isolates of *S. pneumonia and H. influenzae.*

Acute bacterial skin and skin structure infections (ABSSSI) may include cellulitis, erysipelas, wound infections, burns, and major cutaneous abscesses. ABSSSI may present with redness, edema, or induration with lymph node enlargement, purulent drainage or pus within the dermis, and systemic symptoms such as fever.

Common bacterial pathogens causing ABSSSI are *Streptococcus pyogenes* and *Staphylococcus aureus* including methicillin-resistant *Staphylococcus aureus* (MRSA). Less common causes include other *Streptococcus species*, *Enterococcus faecalis*, *Enterococcus faecium*, and Gram-negative bacteria. The incidence of Gram-positive ABSSSI that requires hospitalization has increased along with an increase in antimicrobial resistant organisms. MRSA has become a common cause of ABSSSI infections and pneumonia in the hospital setting. Infections in individuals who lack the usual risk factors for MRSA have also emerged in the community. As a result, community associated MRSA (CA-MRSA) are now a common cause of ABSSSI. Over reliance with use of vancomycin has in addition resulted in emergence of resistant strains of certain bacteria such as Vancomycin resistant *Staphylococcus aureus* (VRSA), Vancomycin intermediate *Staphylococcus aureus* (VISA), and Vancomycin resistant *Enterococcus* (VRE).

As a result of rising prevalence of MRSA, empiric therapy for hospitalized individuals with ABSSSI usually includes intravenous use of an antimicrobial with activity against MRSA and an agent that has activity for the other possible pathogens. Outpatients may be managed with a cost-effective oral agent.

The approach to treatment ASSSSI and pneumonia and antimicrobial selection is guided by manifestation of infection, severity of clinical presentation, location of infection, and results of culture and sensitivities. Other variables to consider in antimicrobial selection include cost, patient risk factors, drug interaction potential, efficacy and safety, monitoring requirements, likely pathogens, and local resistance patterns.

An adequate clinical specimen should be obtained prior to the start of treatment for culture, Gram stain, and *in vitro* susceptibility testing. This is an important step for determining the underlying bacterial etiology of the infection. Once results are known, it may be possible to narrow or change empiric antimicrobial therapy to one that is more cost-effective and one that has specific activity for the microorganism present. Depending upon agent chosen, this may allow for transition from intravenous to oral therapy to facilitate discharge to home for hospitalized individuals who are clinically stable to do so.

Numerous antimicrobials are available for treatment of ABSSSI that have activity against Gram-positive bacteria (including MRSA) as well as the some of the other pathogens involved in the infection. These include vancomycin (IV, generic), daptomycin IV (Cubicin), dalbavacin IV (Dalavance), oritavancin IV (Orbactiv), telavancin IV (Vibativ), ceftaroline IV (Teflaro), tigecycline IV (Tygacil), doxycycline (IV and PO, generic), minocycline (IV and PO), clindamycin (IV and PO, generic), trimethoprim-sulfamethoxazole (IV and PO, generic), linezolid IV and PO (Zyvox), and tedizolid IV and PO (Sivextro).

Antimicrobial agents used for pneumonia can include amoxicillin (high dose), amoxicillin + clavulanate, a cephalosporin, fluoroquinolone (Levofloxacin, moxifloxacin), doxycycline, and a macrolide (azithromycin, erythromycin, clarithromycin).

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Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Community-Acquired Bacterial Pneumonia (CABP) microorganisms susceptible to Nuzyra:

Streptococcus pneumoniae
Staphylococcus aureus (methicillin-susceptible isolates)
Haemophilus influenzae
Haemophilus parainfluenzae
Klebsiella pneumoniae
Legionella pneumophila
Mycoplasma pneumoniae
Chlamydophila pneumoniae

Acute Bacterial Skin and Skin Structure Infections (ABSSSI) microorganisms susceptible to Nuzyra:

Staphylococcus aureus (methicillin-susceptible and -resistant isolates)
Staphylococcus lugdunensis
Streptococcus pyogenes
Streptococcus anginosus grp. (includes *S. anginosus, S. intermedius*, and *S. constellatus*)
Enterococcus faecalis
Enterobacter cloacae
Klebsiella pneumoniae

Acute Bacterial Skin and Skin Structure Infections (ABSSSI):

A bacterial infection of the skin with a lesion size area of at least 75 cm^2 (measured by the area of redness, edema, or induration).

The following infections are defined as ABSSSIs:

Cellulitis/erysipelas: a diffuse skin infection characterized by spreading areas of redness, edema, and/or induration
Wound infection: an infection characterized by purulent drainage from a wound with surrounding redness, edema, and/or induration
Major cutaneous abscess: an infection characterized by a collection of pus within the dermis or deeper that is accompanied by redness, edema, and/or induration

Some Risk factors for Methicillin-resistant staphylococcus aureus infection:

Healthcare-associated factors
Recent hospitalization
Resident of a long-term care facility
Recent surgery
Hemodialysis
Additional factors
HIV infection
Injection drug use
Prior antibiotic use
Factors associated with outbreaks
Incarceration

Military service
Sharing sports equipment
Sharing needles, razors, or other sharp objects

Empiric coverage for Methicillin-resistant staphylococcus aureus (MRSA) includes the following circumstances:

- Systemic signs of toxicity (e.g., fever >100.5°F/38°C, hypotension, or sustained tachycardia)
- Prior episode of MRSA infection or known MRSA colonization
- Lack of clinical response to antibiotic regimen that does not include activity against MRSA
- Presence of risk factor(s) for MRSA infection (including recent hospitalization, residence in a long-term care facility, recent surgery, hemodialysis, IV drug abuse, and HIV infection)
- Proximity of the lesion to an indwelling medical device (e.g., prosthetic joint or vascular graft)

Antimicrobial therapy for treatment of skin and soft tissue infections due to MRSA:

Oral agents	**Parenteral agents**
Preferred agent – choice guided by clinical circumstance, local antibiotic resistance patterns, allergy history, and concomitant medications	
Trimethoprim-sulfamethoxazole	Vancomycin
Doxycycline	Daptomycin
Minocycline	
Clindamycin	
Alternative agent –reserved for patients who do not respond to or cannot tolerate the preferred agent, choice is guided by clinical experience, local antibiotic resistance patterns, adverse effect profile, concomitant medications, and cost	
Linezolid	Linezolid – when stable, transition to oral
Tedizolid	Tedizolid – when stable, transition to oral
Delafloxacin	Delafloxacin – when stable, transition to oral
Omadacycline	Omadacycline – when stable, transition to oral
	Ceftaroline
	Dalbavancin
	Oritavancin
	Telavancin

Resources:

Nuzyra (omadacycline) product information, revised by Paratek Pharmaceuticals, Inc. 03-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 24, 2025.

File TM. Treatment of community-acquired pneumonia in adults in the outpatient setting. In: UpToDate, Ramirez JA, Mitty J, Hussain Z, Bond S (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through October 2025.Topic last updated November 12, 2024. Accessed November 03, 2025.

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Lowry FD. Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Treatment of skin and soft tissue infections. In: UpToDate, Nelson S, Hall KK (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through October 2025. Topic last updated September 30, 2025. Accessed November 03, 2025.

Lowry FD. Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Treatment of bacteremia. In: UpToDate, Tong S, Baron EL (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through October 2025. Topic last updated October 15, 2025. Accessed November 03, 2025.