



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 2/21/2019
LAST REVIEW DATE: 2/17/2022
LAST CRITERIA REVISION DATE: 2/17/2022
ARCHIVE DATE:

NUZYRA™ (omadacycline) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy 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 BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "**Description**" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "**Criteria**" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the [request form](#) in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 2/21/2019
LAST REVIEW DATE: 2/17/2022
LAST CRITERIA REVISION DATE: 2/17/2022
ARCHIVE DATE:

NUZYRA™ (omadacycline) oral tablet

Criteria:

- **Criteria for therapy:** Nuzyra (omadacycline) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:
1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Infectious Disease Specialist
 2. Individual is 18 years of age or older
 3. A confirmed diagnosis of **ONE** of the following:
 - a. Proven or strongly suspected community acquired bacterial pneumonia (CABP) infection caused by susceptible bacteria (See Definitions section)
 - b. Proven or strongly suspected acute bacterial skin and skin structure (ABSSSI) infection caused by susceptible bacteria (See Definitions section)
 - c. When applicable, individual is transitioning intravenous therapy to oral therapy to facilitate a hospital discharge
 4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
 - a. Culture and sensitivity report to identify microorganism and antimicrobial susceptibilities
 5. Individual has failure, contraindication per FDA label or intolerance to **ONE** of the following:
 - a. **For non-hospitalized CABP (one of the following):**
 - i. Beta-lactam plus either a macrolide or doxycycline
 - ii. Monotherapy with a respiratory fluoroquinolone (levofloxacin, moxifloxacin)
 - iii. Monotherapy with an advanced macrolide (azithromycin, clarithromycin)
 - b. **For hospitalized CABP (one of the following):**
 - i. Anti-pneumococcal beta-lactam plus a macrolide (azithromycin or clarithromycin)
 - ii. Monotherapy with a respiratory fluoroquinolone (levofloxacin, moxifloxacin)
 - c. **For CABP with MRSA (one of the following):**
 - i. Linezolid
 - ii. Vancomycin
 - d. **For ABSSSI no MRSA (one of the following):**
 - i. Beta-lactam (ex.: cephalexin, amoxicillin)
 - ii. Trimethoprim-sulfamethoxazole
 - iii. Clindamycin

NUZYRA™ (omadacycline) oral tablet

- e. **For ABSSSI with MRSA, localized mild infection with no systemic symptoms (one of the following):**
 - i. Trimethoprim-sulfamethoxazole
 - ii. Doxycycline
 - iii. Minocycline
- f. **For ABSSSI with MRSA, extensive involvement, rapidly progressing with systemic symptoms or immune compromised (one of the following given first IV then switched to oral):**
 - i. Linezolid
 - ii. Tedizolid
 - iii. Delafloxacin

6. There are no significant interacting drugs

7. There are **NO** FDA-label contraindications, such as:

- a. Known hypersensitivity to tetracycline-class antibacterial drugs

Approval duration:

- 14-days total treatment (includes number of days of in-patient intravenous use)
- **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 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 the following infections caused by susceptible microorganisms: 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.

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



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 2/21/2019
LAST REVIEW DATE: 2/17/2022
LAST CRITERIA REVISION DATE: 2/17/2022
ARCHIVE DATE:

NUZYRA™ (omadacycline) oral tablet

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 ABSSSI 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 describing 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 particular 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), dalbavancin IV (Dalvance), 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).



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 2/21/2019
LAST REVIEW DATE: 2/17/2022
LAST CRITERIA REVISION DATE: 2/17/2022
ARCHIVE DATE:

NUZYRA™ (omadacycline) oral tablet

Definitions:

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 cm² (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

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

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 2/21/2019
LAST REVIEW DATE: 2/17/2022
LAST CRITERIA REVISION DATE: 2/17/2022
ARCHIVE DATE:

NUZYRA™ (omadacycline) oral tablet

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
<i>Preferred agent</i> – choice guided by clinical circumstance, local antibiotic resistance patterns, allergy history, and concomitant medications	
Trimethoprim-sulfamethoxazole	Vancomycin
Doxycycline	Daptomycin
Minocycline	
Clindamycin	
<i>Alternative agent</i> – should be 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



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 2/21/2019
LAST REVIEW DATE: 2/17/2022
LAST CRITERIA REVISION DATE: 2/17/2022
ARCHIVE DATE:

NUZYRA™ (omadacycline) oral tablet

Resources:

Nuzyra (omadacycline) product information, revised by Paratek Pharmaceuticals, Inc. 05-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed December 13, 2021.

File TM. Treatment of community-acquired pneumonia in adults in the outpatient setting. In: UpToDate, Ramirez JA, Bond S (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com>. Topic last updated December 28, 2020. Accessed December 13, 2021.

File TM. Treatment of community-acquired pneumonia in adults who require hospitalization. In: UpToDate, Ramirez JA, Bond S (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com>. Topic last updated September 03, 2021. Accessed December 13, 2021.

Spelman D, Baddour LM. Cellulitis and skin abscess in adults: Treatment. In: UpToDate, Lowy FD, Hall KK (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com>. Topic last updated October 29, 2021. Accessed December 13, 2021.

Lowy FD. Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Treatment of skin and soft tissue infections. In: UpToDate, Spelman D, Hall KK (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com>. Topic last updated May 28, 2021. Accessed December 13, 2021.

Lowy FD. Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Treatment of bacteremia. In: UpToDate, Spelman D, Hall KK (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com>. Topic last updated August 25, 2021. Accessed December 13, 2021.