BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 02/21/19
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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.

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.**

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Criteria:

- **Criteria for initial 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 or is in consultation with Infectious Disease
2. Individual is 18 years of age or older
3. A confirmed diagnosis of **ONE** of the following:
   - Proven or strongly suspected community acquired bacterial pneumonia (CABP) infection caused by susceptible bacteria (See Definitions section)
   - Proven or strongly suspected acute bacterial skin and skin structure (ABSSSI) infection caused by susceptible bacteria (See Definitions section)
   - When applicable, individual is transitioning intravenous therapy to oral therapy to facilitate a hospital discharge
4. Individual has failure, contraindication or intolerance to **ALL** the following preferred step therapy agents:
   - **For CABP non-hospitalized**
     - Beta-lactam **plus** either a macrolide or doxycycline **or** monotherapy with a respiratory fluoroquinolone (moxifloxacin, levofloxacin) **or** monotherapy with an advanced macrolide (azithromycin, clarithromycin)
   - **For CABP hospitalized**
     - Anti-pneumococcal beta-lactam **plus** a macrolide (azithromycin or clarithromycin) **or** monotherapy with a respiratory fluoroquinolone (moxifloxacin, levofloxacin)
   - **For CABP with MRSA**
     - Linezolid or vancomycin
   - **For ABSSSI no MRSA**
     - Beta-lactam or trimethoprim-sulfamethoxazole or clindamycin
   - **For ABSSSI with MRSA, localized mild infection with no systemic symptoms**
     - Trimethoprim-sulfamethoxazole or doxycycline or minocycline
   - **For ABSSSI with MRSA, extensive involvement, rapidly progressing with systemic symptoms or immune compromised**
     - Linezolid or tedizolid or vancomycin
5. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
   - Culture and sensitivity report to identify microorganism and antimicrobial susceptibilities

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6. There are **NO** contraindications
    - Contraindications include:
        - Known hypersensitivity to omadacycline, tetracycline-class antibacterial drugs or any of the excipients of the product

Initial 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

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.

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

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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), 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 + Clavulanate, Cephalosporins, Fluoroquinolone (Levofloxacin, Moxifloxacin), Doxycycline, and a Macrolide (Azithromycin, Erythromycin, Clarithromycin).

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 cm^2 (measured by the area of redness, edema, or induration).

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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

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

Oral agents	Parenteral agents
Clindamycin	Vancomycin
Trimethoprim-sulfamethoxazole	Daptomycin
Doxycycline	Linezolid
Minocycline	Tedizolid
Linezolid	Delafloxacin
Tedizolid	Omadacycline
Delafloxacin	Ceftaroline
Omadacycline	Dalbavancin
	Oritavancin
	Telavancin

Resources:

Nuzyra product information accessed 02-13-19 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=51591524-4703-44c6-8bde-dce3e6a463d1

UpToDate: Treatment of community-acquired pneumonia in adults who require hospitalization. Current through Jan 2019. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-community-acquired-pneumonia-in-adults-who-require-hospitalization?search=community%20acquired%20bacterial%20pneumonia&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

UpToDate: Treatment of community-acquired pneumonia in adults in the outpatient setting. Current through Jan 2019. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-community-acquired-pneumonia-in-adults-in-the-outpatient-setting?search=community%20acquired%20bacterial%20pneumonia&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2

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Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 Update by the Infectious Disease Society of America. CID 2014 DOI: 10.1093/cid/ciu296

UpToDate: Methicillin-resistant staphylococcus aureus (MRSA) in adults: Treatment of skin and soft tissue infections. Current through Jan 2019. https://www-uptodate-com.mwu.idm.oclc.org/contents/methicillin-resistant-staphylococcus-aureus-mrsa-in-adults-treatment-of-skin-and-soft-tissue-infections?search=Skin%20and%20Skin%20Structure%20Infections&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

UpToDate: Cellulitis and skin abscess in adults: Treatment. Current through Jan 2019. https://www-uptodate-com.mwu.idm.oclc.org/contents/cellulitis-and-skin-abscess-in-adults-treatment?search=Skin%20and%20Skin%20Structure%20Infections&topicRef=3176&source=see_link

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.