

# Proposal for ICD-10-PCS Code to Describe Administration of NUZYRA<sup>®</sup> (omadacycline) for injection

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# Agenda

- Overview of Coding Issue
- Unmet Clinical Need and Problem of Rising Antibiotic Resistance
- Overview of NUZYRA<sup>®</sup> (omadacycline) for injection
- The role of NUZYRA in Treatment of Antibiotic-Resistant Infections

# Coding Issue

- There is no unique ICD-10-PCS code to describe the intravenous (IV) administration of NUZYRA® (omadacycline) to treat adult patients with community-acquired bacterial pneumonia (CABP) or acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible microorganisms
- Paratek Pharmaceuticals has filed a New Technology Add-on Payment application (NTAP) for omadacycline for FY 2021

**Paratek recommends the creation of a new ICD-10-PCS code in order to identify and track the administration of omadacycline**

# Antibiotic Resistance Remains a Public Health Crisis

BBC Health  
**Antibiotic resistance plan to fight 'urgent' global threat**  
24 January 2019

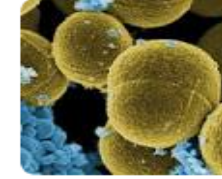


Drug-resistant superbugs are as big a threat as climate change, the health secretary will say as he unveils a new five-year plan to tackle the problem.

CNN International

**Progress on deadly staph infections slows; CDC calls for increased prevention**

(CNN) More than 119,000 people were diagnosed with bloodstream *Staphylococcus aureus* infections in the United States in 2017, and almost ...  
Mar 5, 2019



NBCNews.com

**Antibiotics are losing their power against deadly infections. Can we fix the problem?**

Antibiotics are losing their power against deadly infections. ... can cause infectious bacteria in the body to develop resistance to antibiotics; ...  
4 weeks ago



Administrator Seema Verma ✓  
@SeemaCMS

Our antiquated systems for reimbursing hospitals for antibiotic treatment have disincentivized both the development & use of new antibiotics, leaving doctors powerless to fight off the drastically increasing number of cases of drug resistance.

Washington Times

**Drug-resistant bacteria kill thousands each year**

Drug-resistant bacteria infect millions and kill thousands in the U.S. each year, posing a major threat to the future of health care and treatment ...  
2 weeks ago



# Antibiotic Resistance contributes to poor clinical outcomes and increased healthcare costs

- In the United States, drug-resistant bacteria cause approximately 2 million cases of illnesses and contribute to 23,000 deaths. <sup>1</sup>
- Cost and burden to healthcare dollars, ranges from \$27 billion to \$42 billion annually.<sup>2</sup>
- **CDC Antimicrobial resistance threat levels (2019)<sup>1</sup>:**
  - “Stop referring to a coming post-antibiotic era—it’s already here. You and I are living in a time when some miracle drugs no longer perform miracles and families are being ripped apart by a microscopic enemy. The time for action is now and we can be part of the solution”
  - a) Urgent Threats: *Clostridioides difficile*
  - b) Serious Threats: Drug-resistant *Streptococcus pneumoniae*, Methicillin-resistant *Staphylococcus aureus*
  - c) Concerning Threats: Erythromycin-resistant group A *Streptococcus*, Clindamycin-resistant group B *Streptococcus*

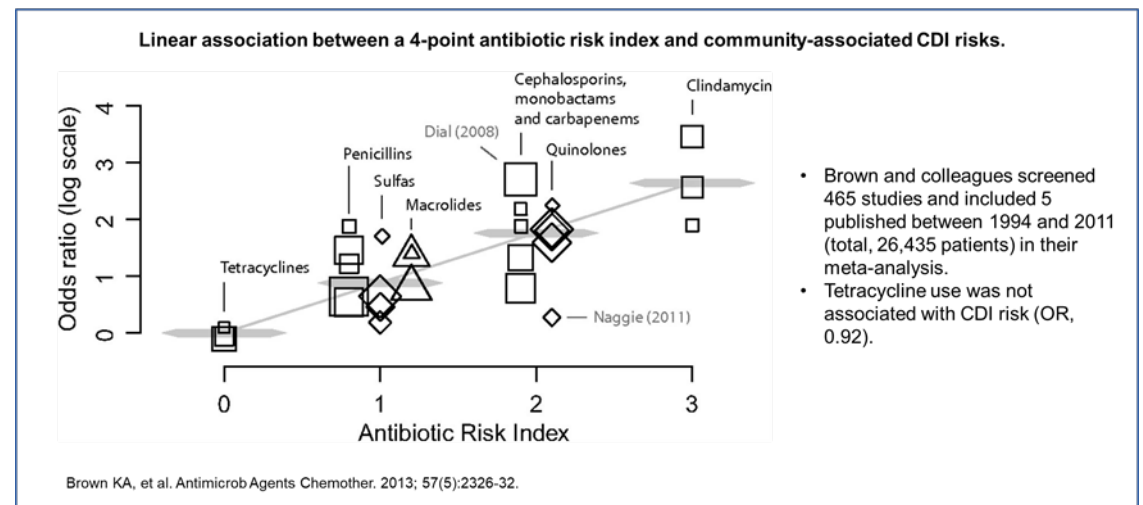
1. CDC’s Antibiotic Resistance Threats in the United States, 2019 (2019 AR Threats Report) <https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf>

2. Ventola CL. The antibiotic resistance crisis: Part 1: Causes and threats. P & T: A Peer-Reviewed Journal for Formulary Management. 2015;40(4):277-283 [PMID: 25859123 PMID: 4378521]

# Example of Improvement in Clinical Outcomes is to Reduce the Risk of *C. Difficile* Infections

- Nearly 223,900 people in the United States required hospital care for *Clostridioides difficile* Infection (CDI) and at least 12,800 people died in 2017.<sup>1</sup>
- CDI is the most frequent cause of mortality associated with gastroenteritis in the healthcare system<sup>2</sup>
  - A 2015 CDC study found that it caused almost half a million infections among patients in the United States in a single year<sup>3</sup>
- Known risk factors for CDI are the use of antibiotics, previous hospitalization, and advanced age (>65 years)<sup>4</sup>
- CDI has been reported with all antibiotic classes, but the risk may differ
  - Antibiotics commonly associated with CDI include fluoroquinolones, cephalosporins, penicillin and clindamycin<sup>5</sup>
  - Lower risk of CDI with tetracyclines<sup>6</sup>

## Antibiotic-Associated CDI Risks



1. The 2019 AR Threats Report is available online at [www.cdc.gov/DrugResistance/Biggest-Threats.html](https://www.cdc.gov/DrugResistance/Biggest-Threats.html)  
2. Johanesen PA, et al. 2015. *Genes (Basel)*, 6: 1347-60. 2. Cohen SH, et al, 2010. *Infect Control Hosp Epidemiol*, 31(5): 431-55.  
3. Lessa FC, et al. *N Engl J Med* 2015; 372:825-834.  
4. Hensgens M, et al. *J Antimicrob Chemother* 2012; 67: 742-748. 5. Deshpande A, et al. *J Antimicrob Chemother* 2013; 68:1951-61. 6. Tariq R, Cho J, Kapoor S, et al. *Clin Infect Dis* 2018; 66(4):514-22.

# NUZYRA<sup>®</sup> (omadacycline) Attributes

- NUZYRA is a once-daily, oral and intravenous antibiotic approved by the Food and Drug Administration (FDA) for treatment of adults with Community-Acquired Bacterial Pneumonia (“CABP”) and Acute-Bacterial Skin and Skin Structure Infection (“ABSSSI”)
- Approved in October of 2018, and granted Priority Review as well as Qualified Infectious Disease Product (QIDP) and Fast Track designations by the FDA
- Commercially available February, 2019
- Modernized tetracycline that is designed to overcome tetracycline resistance
- Broad spectrum of activity against clinically relevant community and multi-drug resistant pathogens that address certain CDC’s unmet needs
  - CDC Serious Threats: Drug-resistant *Streptococcus pneumoniae*, Methicillin-resistant *Staphylococcus aureus*
  - CDC Concerning Threats: Erythromycin-resistant group A *Streptococcus*, Clindamycin-resistant group B *Streptococcus*

# NUZYRA<sup>®</sup> (omadacycline) Overview



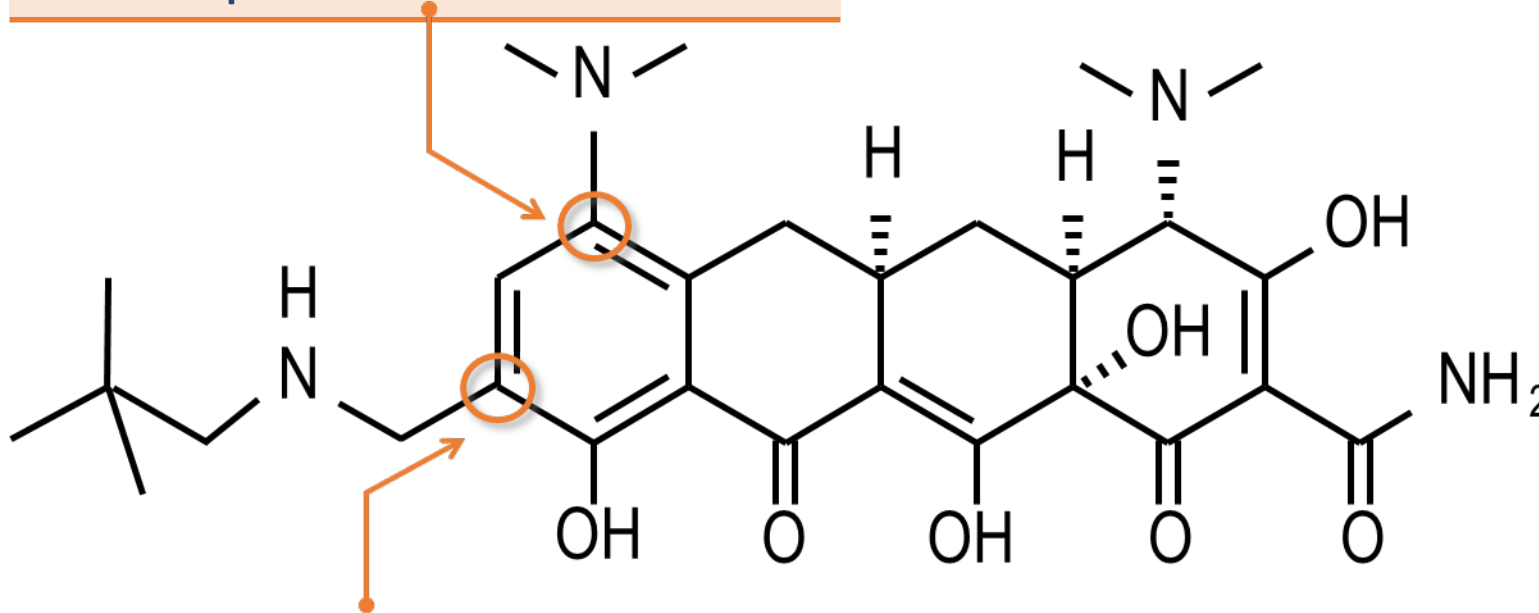
# NUZYRA (omadacycline) Clinical Overview

- Omadacycline was evaluated in three Phase 3 clinical trials
  - These trials included a single Phase 3 trial in CABP patients (OPTIC), and two Phase 3 trials in acute ABSSSI patients (OASIS-1 and OASIS-2)<sup>1</sup>
- **Efficacy in the treatment of adult patients with CABP and ABSSSI<sup>1</sup>**
  - Non-inferior compared to moxifloxacin in the treatment of CABP
  - Non-inferior compared to linezolid in the treatment of ABSSSI
- **Safety profile in 1,073 patients across Phase 3 clinical study program<sup>1</sup>**
  - In the CABP trial, mortality rate of 2% was observed in omadacycline-treated patients compared to 1% in moxifloxacin-treated patients. The cause of the mortality imbalance has not been established
  - The most common adverse reactions (incidence  $\geq 2\%$ ) are nausea, vomiting, infusion site reactions, alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyl transferase increased, hypertension, headache, diarrhea, insomnia, and constipation
  - Low discontinuation (3.1%) and serious adverse events (3.6%) rates

1. NUZYRA Prescribing Information. Paratek Pharmaceuticals, Inc. Boston, MA.

# NUZYRA (omadacycline) Structure

7-Position Modification:  
**Efflux Pump**



9-Position Modification:  
**Ribosomal Protection**

- Amionomethylcycline, which is a semisynthetic tetracycline derivative<sup>1</sup>
- Structural modification on the C-7 and C-9 position to impart common tetracycline resistance mechanisms<sup>1,2</sup>
  - Efflux pump
  - Ribosomal protection

1. Honeyman L, et al. Structure-activity relationship of the aminomethylcyclines and the discovery of omadacycline. *Antimicrob Agents Chemother.* 2015; 59(11):7044-53. 2. Draper MP, et al. Mechanism of action of the novel aminomethylcycline antibiotic omadacycline. *Antimicrob Agents Chemother.* 2014; 58(3):1279-83.

# NUZYRA (omadacycline) Antimicrobial Activity

Omadacycline has been shown to be active against the following bacteria, both *in vitro* and in clinical infections<sup>1</sup>

## CABP Pathogens<sup>2,3</sup>

	N	MIC <sub>90</sub>
<b>Streptococcus pneumoniae</b>	1,066	<b>0.12</b>
<b>Haemophilus influenzae</b>	745	<b>1</b>
<b>Haemophilus parainfluenzae</b>	15	<b>2</b>
<b>Klebsiella pneumoniae</b>	1,564	<b>4</b>
<b>Legionella pneumophila</b>	100	<b>0.25</b>
<b>Chlamydophila pneumoniae</b>	15	<b>0.12-0.25</b>
<b>Mycoplasma pneumoniae</b>	28	<b>0.25</b>

## ABSSSI Pathogens<sup>2</sup>

	N	MIC <sub>90</sub>
<b>Staphylococcus aureus</b>	6,899	<b>0.25</b>
<b>MRSA</b>	2,330	<b>0.25</b>
<b>MSSA</b>	4,569	<b>0.25</b>
<b>Staphylococcus lugdunensis</b>	64	<b>0.12</b>
<b>Streptococcus anginosus group</b>	42	<b>0.12</b>
<b>Streptococcus pyogenes</b>	394	<b>0.12</b>
<b>Enterococcus faecalis</b>	545	<b>0.25</b>
<b>Enterobacter cloacae</b>	324	<b>2</b>

1. NUZYRA Prescribing Information. 2018. Paratek Pharmaceuticals, Inc. Boston, MA.

2. Data on File. Paratek Pharmaceuticals, Inc. JMI Labs. 2016-2017 U.S. Surveillance Data.

3. Data on File. Paratek Pharmaceuticals, Inc. NUZYRA (omadacycline) NDA Submission.

# Dosage and Administration of NUZYRA<sup>®</sup> (omadacycline) for Injection

For treatment of adults with Community Acquired Bacterial Pneumonia (CABP), the recommended dosage regimen of NUZYRA for Injection is as follows (Use NUZYRA for injection administered by intravenous infusion for the loading dose in CABP patients):

Loading Dose	Maintenance Dose	Treatment Duration
200-mg by intravenous infusion over 60 minutes on the 1 <sup>st</sup> day.	100-mg by intravenous infusion once daily infused over 30 minutes.	7 to 14 Days

For treatment of adults Acute Bacterial Skin Structure and Skin Infection (ABSSSI), the recommended dosage regimen of NUZYRA for injection is as follows (Use NUZYRA for injection administered by intravenous infusion or NUZYRA tablets orally administered for the loading dose in ABSSSI patients):

Loading Dose	Maintenance Dose	Treatment Duration
200-mg by intravenous infusion over 60 minutes on the 1 <sup>st</sup> day.	100-mg by intravenous infusion once daily infused over 30 minutes.	7 to 14 Days

# Summary of Attributes

NUZYRA® (omadacycline) is an aminomethylcycline antibiotic available in an oral and intravenous formulation designed to overcome tetracycline resistance. NUZYRA offers an alternative when other antibiotics may not be a clinical option

Monotherapy	No dosage adjustment for hepatic or renally impaired patients	Covers community and multi-drug resistant pathogens	Facilitates transitions of care to decrease length of hospital stay
Once-a day			
No cases of <i>Clostridioides difficile</i> infections reported throughout the development program	Tetracyclines are established as safe and tolerable	Minimal drug-drug interaction*	No QTC prolongation
			Alternative to fluroquinolones

\*Anticoagulation monitoring, antacids and cations with oral formulation