Nuzyra™ (omadacycline) – New drug approval

- On October 2, 2018, Paratek Pharmaceuticals announced the FDA approval of Nuzyra (omadacycline), 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 infections (ABSSSI).

    - Susceptible microorganisms for CABP include Streptococcus pneumoniae, Staphylococcus aureus (methicillin-susceptible isolates), Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Legionella pneumophila, Mycoplasma pneumoniae, and Chlamydophila pneumoniae.
    - Susceptible microorganisms for ABSSSI include 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, and Klebsiella pneumoniae.

- The Centers for Disease Control and Prevention estimates that drug-resistant bacteria cause 2 million illnesses and approximately 23,000 deaths each year in the U.S. The main bacteria causing CABP, *Streptococcus pneumoniae*, is responsible for 1.2 million infections and 7,000 deaths, whereas ABSSSI is responsible for more than 750,000 hospitalizations.

- Nuzyra is a modernized tetracycline, specifically designed to overcome tetracycline resistance and exhibits activity across a spectrum of bacteria, including Gram-positive, Gram-negative, atypicals, and other drug-resistant strains.

- The efficacy of Nuzyra for the treatment of CABP was demonstrated in 774 adult patients receiving Nuzyra or moxifloxacin. Patients received at least three days of intravenous (IV) therapy followed by IV or oral therapy for a total of 7 – 14 days. Clinical success at 72 – 120 hours after the first dose, was defined as survival with improvement in at least two of four symptoms (cough, sputum production, chest pain, dyspnea) and clinical response at 5 – 10 days after therapy was defined as survival and improvement in signs and symptoms of CABP with no further antibacterial therapy needed.

    - Clinical success was seen in 81.1% of Nuzyra-treated patients vs. 82.7% of moxifloxacin-treated patients (Difference: -1.6 [95% CI: -7.1, 3.8]).
    - Clinical response was seen in 87.6% of Nuzyra-treated patients vs. 85.1% of moxifloxacin-treated patients (Difference: 2.5 [95% CI: -2.4, 7.4]).

- The efficacy of Nuzyra for the treatment of ABSSSI was evaluated in two studies enrolling 1,390 patients. Patients received 7 – 14 days of therapy with Nuzyra or linezolid. In the first study, patients started with IV therapy, with the option to switch to oral therapy. In the second study, patients only received oral therapy. In both studies, efficacy was determined by the successful early clinical response at 48 – 72 hours after the first dose (defined as a $\geq$ 20% decrease in lesion size) and clinical response at 7 – 14 days after the last dose (defined as survival after completion of study treatment without receiving any alternative antibacterial therapy, without unplanned major surgical intervention, and sufficient resolution of infection).

    - In the first study, 84.8% of the Nuzyra-treated patients experienced successful early clinical response vs. 85.5% of the linezolid-treated patients (Difference: -0.7 [95% CI: -6.3, 4.9]). Clinical response at 7 – 14 days after the last dose was achieved in 86.1% of the Nuzyra-treated patients vs. 83.6% of the linezolid-treated patients (Difference: 2.5 [95% CI: -3.2, 8.2]).

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— In the second study, 87.3% of the Nuzyra-treated patients experienced successful early clinical response vs. 82.2% of the linezolid-treated patients (Difference: 5.1 [95% CI: -0.2, 10.5]). Clinical response at 7 – 14 days after the last dose was achieved in 83.9% of the Nuzyra-treated patients vs. 80.5% of the linezolid-treated patients (Difference: 3.4 [95% CI: [-2.3, 9.1]).

- Warnings and precautions of Nuzyra include mortality imbalance in patients with CABP, tooth discoloration and enamel hypoplasia, inhibition of bone growth, hypersensitivity reactions, *Clostridium difficile*-associated diarrhea, tetracycline class effects, and development of drug-resistant bacteria.

- The most common adverse reactions (≥ 2%) with Nuzyra use were nausea, vomiting, infusion site reactions, increased alanine aminotransferase, increased aspartate aminotransferase, increased gamma-glutamyl transferase, hypertension, headache, diarrhea, insomnia, and constipation.

- The recommended loading dose of Nuzyra is given IV and maintenance dose is given IV or oral in adult patients with CABP as follows:

Loading Doses	Maintenance Dose	Treatment Duration
200 mg by IV infusion over 60 minutes on day 1. Or 100 mg by IV infusion over 30 minutes, twice on day 1.	100 mg by IV infusion over 30 minutes once daily. Or 300 mg orally once daily.	7 – 14 days

- The recommended loading and maintenance doses of Nuzyra may be given IV or oral in adult patients with ABSSSI as follows:

Loading Doses	Maintenance Dose	Treatment Duration
200 mg by IV infusion over 60 minutes on day 1. Or 100 mg by IV infusion over 30 minutes, twice on day 1.	100 mg by IV infusion over 30 minutes once daily. Or 300 mg orally once daily.	7 – 14 days
450 mg orally once a day on day 1 and day 2.	300 mg orally once daily.	

- Paratek Pharmaceuticals plans to launch Nuzyra in the first quarter of 2019. Nuzyra will be available as a 100 mg single-dose vial for injection and as a 150 mg tablet.