CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

209816Orig1s000
209817Orig1s000

Trade Name:	NUZYRA tablets, 150 mg NUZYRA for injection, 100 mg
Generic or Proper Name:	omadacycline
Sponsor:	Paratek Pharmaceuticals, Inc
Approval Date:	October 2, 2018
Indication:	For the treatment of Community-Acquired Bacterial Pneumonia (CABP) and Acute Bacterial Skin and Skin Structure Infections (ABSSSI) in adults due to the designated susceptible bacteria.

CENTER FOR DRUG EVALUATION AND RESEARCH

209816Orig1s000
209817Orig1s000

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	**X**
Other Action Letters	
Labeling	**X**
REMS	
Officer/Employee List	**X**
Multidiscipline Review(s) • **Summary Review** • **Office Director** • **Cross Discipline Team Leader** • **Clinical** • **Non-Clinical** • **Statistical** • **Clinical Pharmacology**	**X**
Product Quality Review(s)	**X**
Clinical Microbiology / Virology Review(s)	
Other Reviews	**X**
Risk Assessment and Risk Mitigation Review(s)	**X**
Proprietary Name Review(s)	**X**
Administrative/Correspondence Document(s)	**X**

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APPLICATION NUMBER:

209816Orig1s000
209817Orig1s000

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 209816
NDA 209817

NDA APPROVAL

Paratek Pharmaceuticals, Inc.
Attention: Randall Brenner
Head, Regulatory Affairs, Quality and Technical Operations
1000 First Avenue, Suite 200
King of Prussia, PA 19406

Dear Mr. Brenner:

Please refer to your New Drug Applications (NDAs) dated February 02, 2018, received February 02, 2018, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for NUZYRA (omadacycline) tablets, 150 mg (NDA 209816) and NUZYRA (omadacycline) for injection, 100 mg (NDA 209817).

These new drug applications provide for the use of NUZYRA (omadacycline) tablets, 150 mg and NUZYRA (omadacycline) for injection, 100 mg, for the treatment of Community-Acquired Bacterial Pneumonia (CABP) and Acute Bacterial Skin and Skin Structure Infections (ABSSSI) in adults due to the designated susceptible bacteria.

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the Prescribing Information, as well as annual reportable changes not included in the enclosed labeling. Information on submitting

SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human PharmaceuticalProduct Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3).* For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 209816 and 209817**." Approval of this submission by FDA is not required before the labeling is used.

MARKET PACKAGE

Please submit one market package for each of the drug products when they are available to the following address:

Deepak Aggarwal
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 6211
10903 New Hampshire Avenue
Silver Spring, Maryland

Use zip code **20903** *if shipping via United States Postal Service (USPS).*
Use zip code **20993** *if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to < 8 years because there is nonclinical evidence strongly suggesting that omadacycline would be unsafe in this pediatric

group due to the risk of tetracycline-associated tooth discoloration and enamel hypoplasia, and the risk of tetracycline-associated inhibition of bone growth.

We are deferring submission of your pediatric studies for ages 8 to < 18 years for these applications because these products are ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(C) of the FDCA. These required studies are listed below.

3487-1 Conduct a single dose pharmacokinetic and safety study in children ages 8 to 17 years who are receiving antibacterial drug therapy for an infectious disease.

The timetable you submitted on October 01, 2018 states that you will conduct this study according to the following schedule:

Draft protocol:	05/2019
Final protocol:	08/2019
Study completion:	12/2020
Final report:	05/2021

3487-2 Conduct an active-controlled safety study in children 8-17 years who have acute bacterial skin and skin structure infections.

The timetable you submitted on October 01, 2018 states that you will conduct this study according to the following schedule:

Draft protocol:	11/2020
Final protocol:	02/2021
Study Completion:	12/2023
Final report:	05/2024

3487-3 Conduct an active-controlled safety study in children 8-17 years who have community-acquired bacterial pneumonia.

The timetable you submitted on October 01, 2018 states that you will conduct this study according to the following schedule:

Draft protocol:	03/2023
Final protocol:	06/2023
Study completion:	12/2025
Final report:	03/2026

Submit the protocol(s) to your INDs 073431 and 075928, with a cross-reference letter to the NDAs.

Reports of these required pediatric postmarketing studies must be submitted as supplements to your approved NDAs with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submissions "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submissions.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify the serious risk of mortality imbalance in patients with CABP and the development of resistance to NUZYRA (omadacycline) in microorganisms specific to the CABP and ABSSSI indications in the label.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks. Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

3487-4 Conduct an active-controlled safety and efficacy study in adults with community-acquired bacterial pneumonia

The timetable you submitted on October 01, 2018 states that you will conduct this study according to the following schedule:

Draft protocol:	01/2019
Final protocol:	03/2019
Study Completion:	11/2022
Final report:	04/2023

3487-5 Conduct a United States surveillance study for 5 years from the date of marketing to determine if resistance to NUZYRA (omadacycline) has developed in those organisms specific to the indications in the label.

The timetable you submitted on September 25, 2018 states that you will conduct this study according to the following schedule:

Final protocol submission:	12/2018
First interim report:	05/2020
Second interim report:	05/2021
Third interim report:	05/2022
Fourth interim report:	05/2023
Fifth interim report:	05/2024
Study completion date:	12/2023
Final report submission date:	05/2024

Submit the clinical protocols to your INDs 073431 and 075928 with a cross-reference letter to these NDAs. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final reports to your NDAs. Prominently identify the submissions with the following wording in bold capital letters at the top of the first page of each submission, as appropriate: **Required Postmarketing Protocol Under 505(o), Required Postmarketing Final Report Under 505(o), Required Postmarketing Correspondence Under 505(o).**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the Prescribing Information, Medication Guide, and Patient Package Insert (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for these applications.

If you have any questions, call Deepak Aggarwal, MS, MSPH, Regulatory Project Manager, at 301-796-0746.

Sincerely,

{See appended electronic signature page}

Edward M. Cox, MD, MPH
Director
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Carton and Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

EDWARD M COX
10/02/2018