DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206334

NDA APPROVAL

The Medicines Company
Attention: Ketna Patel, PharmD
Director, Regulatory Affairs
8 Sylvan Way
Parsippany, NJ 07054

Dear Dr. Patel:

Please refer to your New Drug Application (NDA) dated December 6, 2013, received December 6, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Orbactiv (oritavancin diphosphate) Lyophilized Powder for Injection, 400 mg/vial.

We acknowledge receipt of your amendments dated December 13, 19 and 26; January 3, 10, and 23; February 12, 19, and 21; March 5, 7 and 21; April 4 (2) and 9; May 9 and 28 (2); June 25 and 27; July 9, 10, 11, 14, and 17; and August 4, 5, and 6, 2014.

This new drug application provides for the use of Orbactiv (oritavancin diphosphate) Lyophilized Powder for Injection in the treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI).

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

We note that your August 6, 2014, submission includes final printed labeling (FPL) for your package insert. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

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 package insert. 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 IMMEDIATE CONTAINER LABELS

We acknowledge your August 6, 2014, submission containing final printed carton and container labels.

Marketing the product that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

ADVISORY COMMITTEE

Your application for Orbactiv (oritavancin diphosphate) was not referred to an FDA advisory committee because the application did not raise significant public health questions on the role of the drug in the diagnosis, cure, mitigation, treatment, or prevention of a disease and outside expertise was not necessary; there were no controversial issues that would benefit from advisory committee discussion.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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 deferring submission of your pediatric studies for ages 0 to 17 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required under 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)(B) of the FDCA. These required studies are listed below:

2165-1 Conduct an open-label, dose-finding, pharmacokinetics, safety and tolerability study of Orbactiv (oritavancin diphosphate) single dose infusion in pediatric subjects less than 18 years of age with suspected or confirmed bacterial infections.

The timetable you submitted on July 10, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submitted:	December 16, 2013
Study Completion:	03/17
Final Report Submission:	09/17

2165-2 Conduct a multicenter, evaluator-blind, randomized study to evaluate the safety and tolerability of single-dose IV Orbactiv (oritavancin diphosphate) versus vancomycin for the treatment of pediatric subjects less than 18 years of age with acute bacterial skin and skin structure infections.

The timetable you submitted on July 10, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	09/17
Study Completion:	07/20
Final Report Submission:	12/20

Submit the protocols to your IND 51292, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA 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 submission **"SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS"** in large font, bolded type at the beginning of the cover letter of the submission.

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 development of resistance to Orbactiv (oritavancin diphosphate) in organisms specific to the ABSSSI indication 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 this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

2165-3 Conduct a US surveillance study over a five-year period from the date of marketing Orbactiv (oritavancin diphosphate) to determine if resistance to

oritavancin has developed in those organisms specific to the indication in the label for ABSSSI.

The timetable you submitted on July 9, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submitted:	July 9, 2014
First interim report:	04/15
Second interim report:	04/16
Third interim report:	04/17
Fourth interim report:	04/18
Fifth interim report:	04/19
Study completion:	12/19
Final report submission:	04/20

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess a known serious risk of bleeding due to interaction with concomitant warfarin therapy and interference of Orbactiv (oritavancin diphosphate) with coagulation tests.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

2165-4 Conduct an open label trial evaluating the safety of a single 1200 mg IV dose of Orbactiv (oritavancin diphosphate) in patients on concomitant chronic warfarin therapy who are being treated for ABSSSI.

The timetable you submitted on August 5, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	12/14
Trial Completion:	05/16
Final Report Submission:	08/16

2165-5 Conduct an open-label trial to assess the clinical significance of the drug-drug interaction between a single 1200 mg IV dose of Orbactiv (oritavancin diphosphate) and warfarin in healthy volunteers.

The timetable you submitted on August 5, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	11/14
Trial Completion:	04/15
Final Report Submission:	06/15

2165-6 Conduct a single-center, open-label trial to evaluate the effects of a single 1200 mg IV dose of Orbactiv (oritavancin diphosphate) on the results of multiple coagulation tests in healthy volunteers.

The timetable you submitted on August 5, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	10/14
Trial Completion:	03/15
Final Report Submission:	05/15

Submit the protocol to your IND 51292, with a cross-reference letter to this NDA. Submit the final report to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the 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. 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). 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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

2165-7 Conduct a study to evaluate the effects of oritavancin on phospholipid and non-phospholipid based coagulation tests in vitro.

The timetable you submitted on August 5, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	9/14
Study Completion:	4/15
Final Report Submission:	4/15

Submit clinical protocols to your IND 51292 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

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 package insert to:

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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, 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 biologics 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 this application.

PDUFA V APPLICANT INTERVIEW

FDA has contracted with Eastern Research Group, Inc. (ERG) to conduct an independent interim and final assessment of the Program for Enhanced Review Transparency and Communication for NME NDAs and Original BLAs under PDUFA V ('the Program'). The PDUFA V Commitment Letter states that these assessments will include interviews with applicants following FDA action on applications reviewed in the Program. For this purpose, first-cycle actions include approvals, complete responses, and withdrawals after filing. The purpose of the interview is to better understand applicant experiences with the Program and its ability to improve transparency and communication during FDA review.

ERG will contact you to schedule a PDUFA V applicant interview and provide specifics about the interview process. Your responses during the interview will be confidential with respect to the FDA review team. ERG has signed a non-disclosure agreement and will not disclose any identifying information to anyone outside their project team. They will report only anonymized results and findings in the interim and final assessments. Members of the FDA review team will be interviewed by ERG separately. While your participation in the interview is voluntary, your feedback will be helpful to these assessments.

If you have any questions, call Naseya Minor, Regulatory Project Manager, at (301) 796-0756.

Sincerely,

{See appended electronic signature page}

John J. Farley, MD, MPH
Deputy 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 and this page is the manifestation of the electronic signature.

/s/

JOHN J FARLEY
08/06/2014