DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21-883

NDA APPROVAL

Durata Therapeutics International, B.V.
c/o Durata Therapeutics, Inc.
Attention: Briton Shell, PhD
Director, Regulatory Affairs, North America
322 East Main Street, 3rd Floor
Branford, CT 06405

Dear Dr. Shell:

Please refer to your New Drug Application (NDA) dated September 26, 2013, received September 26, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Dalvance (dalbavancin hydrochloride) Lyophilized Powder for Injection, 500 mg.

We acknowledge receipt of your amendments dated September 30, October 16, 21, and 25, November 1, 5, 8, 14, 22, 25, 26 and 27, December 5, 11, 16, 20, 2013, and January 2, 8, 9, 20, 21 and 24, February 14 and 24, March 6, 13, 14 (2), 18 and 28, April 1, 7, 10, 14 and 22, and May 6, 7, 8, 13, 15 (3), 16, 19, 21 and 22, 2014.

This new drug application provides for the use of Dalvance (dalbavancin hydrochloride) 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.

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. 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

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels submitted on April 1, 2014, 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 *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 21-883**." Approval of this submission by FDA is not required before the labeling is used.

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

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(s) 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 until June 30, 2020, because this product is 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)(B) of the FDCA. These studies are listed below:

2145-1: Conduct a single dose pharmacokinetic (PK) study in children from 3 months to less than 12 years of age.

The timetable you submitted on May 22, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	May 2013 (submitted)
Study Completion:	March 2015
Final Report Submission:	September 2015

2145-2: Conduct a single dose PK study in neonates/infants from 0 to less than 3 months of age.

The timetable you submitted on May 22, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	May 2015
Study Completion:	November 2016
Final Report Submission:	May 2017

2145-3: Conduct a Phase 3, randomized, comparator-controlled study of dalbavancin in children from 3 months to 17 years of age with ABSSSI.

The timetable you submitted on May 22, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	December 2014
Study Completion:	December 2016
Final Report Submission:	June 2017

2145-4: Conduct a Phase 3, randomized, comparator-controlled study of dalbavancin in neonates/infants from birth to less than 3 months of age with ABSSSI.

The timetable you submitted on May 22, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	December 2016
Study Completion:	December 2019
Final Report Submission:	June 2020

Submit the protocols to your IND 60,613, with a cross-reference letter to NDA 21-883.

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 Dalvance (dalbavancin hydrochloride) 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:

2145-5: Conduct US surveillance studies for five years from the date of marketing DALVANCE to determine if resistance to dalbavancin has developed in those organisms specific to the indication in the label for ABSSSI.

The timetable you submitted on May 22, 2014, states that you will conduct this study according to the following schedule:

Final protocol submission:	September 2014
First interim report:	March 2016
Second interim report:	March 2017
Third interim report:	March 2018
Fourth interim report:	March 2019
Fifth interim report:	March 2020
Study completion date:	September 2019
Final report submission:	September 2020

2145-6: Conduct studies to define the mechanism(s) of resistance for isolates identified as being resistant to dalbavancin during the surveillance period (five years from the date of marketing).

The timetable you submitted on May 22, 2014, states that you will conduct this study according to the following schedule:

Final protocol submission:	September 2014
First interim report:	March 2016
Second interim report:	March 2017

Third interim report:	March 2018
Fourth interim report:	March 2019
Fifth interim report:	March 2020
Study completion date:	September 2019
Final report submission:	September 2020

Submit the protocols to your IND 60,613, with a cross-reference letter to this NDA. Submit all final reports 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. 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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

2145-7: Replace [redacted] (b) (4) used for preparing the Master Cell Bank with a [redacted] (b) (4)

The timetable you submitted on May 22, 2014, states that you will report on this commitment according to the following schedule:

Interim Report Submission:	June 2015
Final Report Submission:	June 2016

2145-8: Submit batch release test results from upcoming process performance qualification lot(s) when process performance qualification activities have been completed.

The timetable you submitted on May 22, 2014, states that you submit the final report for this commitment according to the following schedule:

Final Report Submission: November 2014

Submit clinical protocols to your IND 60,613 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all 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 this postmarketing commitment 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 J. Christopher Davi, MS, Senior Regulatory Project Manager at (301) 796-0702.

Sincerely,

{See appended electronic signature page}

John Farley, MD, MPH
Deputy Director
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosures: 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
05/23/2014