

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

021883Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 21-883

SUPPL # N/A

HFD # 520

Trade Name: DALVANCE

Generic Name: Dalbavancin Hydrochloride, Lyophilized Powder for Injection, 500 mg

Applicant Name: Durata Therapeutics, B.V.

Approval Date: May 23, 2014

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

N/A

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

N/A

d) Did the applicant request exclusivity?

YES

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

5 years NCE plus 5 years GAIN exclusivity extension

e) Has pediatric exclusivity been granted for this Active Moiety?

NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

N/A

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a)

is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

Investigation #1
!
!
YES ! NO
Explain: ! Explain:

Investigation #2
!
!
YES ! NO
Explain: ! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES NO

If yes, explain:

=====
Name of person completing form: J. Christopher Davi
Title: Senior Regulatory Project Manager
Date: May 27, 2014

Name of Office/Division Director signing form: Sumathi Nambiar, MD, MPH
Title: Division Director, DAIP
Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

APPENDIX – GAIN EXCLUSIVITY SUMMARY

GAIN Exclusivity Summary

1. Does this product have Qualified Infectious Disease Product (QIDP) designation?

YES

2. Is the indication(s) approved in this NDA or supplement the same as the indication(s) identified in the QIDP designation letter?

YES

3. Has this product or any product containing this drug previously received a 5-year GAIN exclusivity extension?

NO

Name of person completing form: J. Christopher Davi, MS

Title: Senior Regulatory Project Manager

Date: May 27, 2014

Name of Office/Division Director signing form: Sumathi Nambiar, MD, MPH

Title: Division Director, DAIP

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JOSEPH C DAVI
05/27/2014

SUMATHI NAMBIAR
05/27/2014

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 21-883 BLA # N/A	NDA Supplement # N/A BLA Supplement # N/A	If NDA, Efficacy Supplement Type: N/A <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: Dalvance Established/Proper Name: Dalbavancin hydrochloride Dosage Form: Injection		Applicant: Durata Therapeutics, B.V., Amsterdam Agent for Applicant (if applicable): Durata Therapeutics, Inc.
RPM: J. Christopher Davi, MS, Sr. RPM, DAIP		Division: DAIP
NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) BLA Application Type: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a) Efficacy Supplement: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a)		For ALL 505(b)(2) applications, two months prior to EVERY action: <ul style="list-style-type: none"> Review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) <ul style="list-style-type: none"> <input type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity (<i>notify CDER OND IO</i>) Date of check: _____ <i>Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</i>
❖ Actions		
<ul style="list-style-type: none"> Proposed action: May 23, 2014 User Fee Goal Date is May 26, 2014 		X AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> Previous actions (<i>specify type and date for each action taken</i>) 		September 21, 2005 (AE) June 21, 2006 (AE) December 20, 2007 (AE)
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____		N/A
❖ Application Characteristics ³		

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

² For resubmissions, (b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

Review priority: Standard Priority
 Chemical classification (new NDAs only): Type 1 (NME)
(confirm chemical classification at time of approval)

- Fast Track Rx-to-OTC full switch
 Rolling Review Rx-to-OTC partial switch
 Orphan drug designation Direct-to-OTC
 Breakthrough Therapy designation

- NDAs: Subpart H Accelerated approval (21 CFR 314.510)
 Restricted distribution (21 CFR 314.520)
 Subpart I Approval based on animal studies
- BLAs: Subpart E Accelerated approval (21 CFR 601.41)
 Restricted distribution (21 CFR 601.42)
 Subpart H Approval based on animal studies

- Submitted in response to a PMR
 Submitted in response to a PMC
 Submitted in response to a Pediatric Written Request
- REMS: MedGuide
 Communication Plan
 ETASU
 MedGuide w/o REMS
 REMS not required

Comments: None

❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	N/A
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)	N/A
❖ Public communications (<i>approvals only</i>)	
• Office of Executive Programs (OEP) liaison has been notified of action	X Yes <input type="checkbox"/> No
• Indicate what types (if any) of information were issued	<input type="checkbox"/> None <input checked="" type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)? • If so, specify the type	No
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	Verified
CONTENTS OF ACTION PACKAGE	
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	Included
Documentation of consent/non-consent by officers/employees	Included

Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Included; May 23, 2014 (AP) September 21, 2005 (AE) June 21, 2006 (AE) December 20, 2007 (AE)
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
• Most recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>)	Included
• Original applicant-proposed labeling	Included (September 26, 2013)
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>)	None
• Most-recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>)	None
• Original applicant-proposed labeling	None
❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)	
• Most-recent draft labeling	Included (April 1, 2014)
❖ Proprietary Name	November 26, 2013
• Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)	“Dalvance” trade name acceptable (DMEPA Review dated November 25, 2013)
• Review(s) (<i>indicate date(s)</i>)	
❖ Labeling reviews (<i>indicate dates of reviews</i>)	DMPP/PLT (DRISK): March 7, 2014 OPDP: April 11, 2014 DMEPA: February 28, 2014 DAIP RPM: May 13, 2014
Administrative / Regulatory Documents	
❖ Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)	RPM Filing Review: Included
❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Committee	N/A
❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)	Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	No

⁴ Filing reviews for scientific disciplines should be filed with the respective discipline.

<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	N/A
❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <u>April 9, 2014</u> If PeRC review not necessary, explain: <u>N/A</u> 	
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters) (<i>do not include previous action letters, as these are located elsewhere in package</i>)	Included
❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)	Included
❖ Minutes of Meetings	
<ul style="list-style-type: none"> • If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>) 	None
<ul style="list-style-type: none"> • Pre-NDA/BLA meeting (<i>indicate date of mtg</i>) 	No Meeting
<ul style="list-style-type: none"> • EOP2 meeting (<i>indicate date of mtg</i>) 	No Meeting
<ul style="list-style-type: none"> • Mid-cycle Communication (<i>indicate date of mtg</i>) 	January 15, 2014
<ul style="list-style-type: none"> • Late-cycle Meeting (<i>indicate date of mtg</i>) 	March 20, 2014
<ul style="list-style-type: none"> • Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>) 	None
❖ Advisory Committee Meeting(s)	Yes
<ul style="list-style-type: none"> • Date(s) of Meeting(s) 	March 31, 2014
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	May 23, 2104
Division Director Summary Review (<i>indicate date for each review</i>)	May 23, 2014
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	May 16, 2014
PMR/PMC Development Templates (<i>indicate total number</i>)	May 20 & 22, 2014 (2)
Clinical	
❖ Clinical Reviews	
<ul style="list-style-type: none"> • Clinical Team Leader Review(s) (<i>indicate date for each review</i>) 	May 16, 2014 (CDTL Review)
<ul style="list-style-type: none"> • Clinical review(s) (<i>indicate date for each review</i>) 	April 3, 2014 September 21, 2005 (2) May 18, 2006 December 11, 2007
<ul style="list-style-type: none"> • Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>) 	None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	April 3, 2014 (Pages 111-112 of clinical review)
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	N/A

❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	N/A
❖ Risk Management <ul style="list-style-type: none"> REMS Documents and REMS Supporting Document (<i>indicate date(s) of submission(s)</i>) REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) 	N/A March 7, 2014 None
❖ OSI Clinical Inspection Review Summary(ies) (<i>include copies of OSI letters to investigators</i>)	Included
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	No separate review
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	February 26, 2014 September 19, 2005 May 17, 2006
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	No separate review
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	No separate review
Statistical Review(s) (<i>indicate date for each review</i>)	May 13, 2014 September 20, 2005 December 12, 2007 December 18, 2007
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	No separate review
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	No separate review
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	March 4, 2014 September 20, 2005
❖ OSI Clinical Pharmacology Inspection Review Summary (<i>include copies of OSI letters</i>)	Included
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	May 16, 2014
• Supervisory Review(s) (<i>indicate date for each review</i>)	No separate review
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	March 1, 2014 February 24, 2006
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	None
❖ ECAC/CAC report/memo of meeting	None
❖ OSI Nonclinical Inspection Review Summary (<i>include copies of OSI letters</i>)	None requested

Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>	No separate review
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>	No separate review
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>	February 26, 2014 (CMC PQR) March 24, 2014 (Biopharm) May 16, 2014 (CMC PQR) September 21, 2005 (CMC PQR) May 24, 2006 (CMC PQR) November 2, 2007 (CMC PQR)
❖ Microbiology Reviews X NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i> <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>	December 24, 2013 May 19, 2005 October 22, 2007
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>	None
❖ Environmental Assessment (check one) (original and supplemental applications)	
X Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>	February 26, 2014 (CMC PQR)
<input type="checkbox"/> Review & FONSI <i>(indicate date of review)</i>	N/A
<input type="checkbox"/> Review & Environmental Impact Statement <i>(indicate date of each review)</i>	N/A
❖ Facilities Review/Inspection	
X NDAs: Facilities inspections (include EER printout or EER Summary Report only; do NOT include EER Detailed Report; date completed must be within 2 years of action date) <i>(only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁵)</i>	Date completed: May 22, 2014 X Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (date of most recent TB-EER must be within 30 days of action date) <i>(original and supplemental BLAs)</i>	N/A
❖ NDAs: Methods Validation <i>(check box only, do not include documents)</i>	May 15, 2014 (Summary Report)

⁵ i.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Day of Approval Activities	
❖ For all 505(b)(2) applications: • Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)	N/A
• Finalize 505(b)(2) assessment	N/A
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	X Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	X Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	X Done
❖ Ensure Pediatric Record is accurate	X Done
❖ Send approval email within one business day to CDER-APPROVALS	X Done

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JOSEPH C DAVI
05/29/2014



NDA 21-883

MID-CYCLE COMMUNICATION

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) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Dalbavancin for Injection.

We also refer to the teleconference between representatives of your firm and the FDA on January 15, 2014. The purpose of the teleconference was to provide you with an update on the status of the review of your application.

A record of the teleconference is enclosed for your information.

If you have any questions, call J. Christopher Davi, MS, Senior Regulatory Project Manager, at (301) 796-0702.

Sincerely,

{See appended electronic signature page}

Maureen Dillon-Parker
Chief, Project Management Staff
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Mid-Cycle Communication Minutes



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MID-CYCLE COMMUNICATION

Meeting Date and Time: January 15, 2014/1:00pm

Application Number: NDA 21-883
Product Name: Dalbavancin for Injection
Indication: ABSSSI
Applicant Name: Durata Therapeutics International, BV

Meeting Chair: Sumathi Nambiar, MD, MPH
Meeting Recorder: J. Christopher Davi, MS

FDA ATTENDEES (DAIP unless otherwise noted):

Sumathi Nambiar, MD, MPH, Director
Katherine A. Laessig, MD, Deputy Director
John J. Alexander, MD, MPH, Medical Team Leader
Dmitri Iarikov, MD, Medical Reviewer
Chris Kadoorie, PhD, Biostatistics Reviewer
Yvette Waples, Senior Regulatory Manager, Advisory and Consultants Staff
Jennifer Shepherd, RPh, Senior Regulatory Manager, Advisory and Consultants Staff
David L. Roeder, MS, Associate Director of Regulatory Affairs, OAP
Maureen Dillon-Parker, Chief, Project Management Staff
J. Christopher Davi, MS, Senior Regulatory Project Manager
Christopher Sese, FDA Contractor, Eastern Research Group, Inc.

APPLICANT ATTENDEES (Durata Therapeutics International, BV):

Michael Dunne, MD, Chief Medical Officer
Sailaja Puttagunta, MD, Executive Director of Clinical and Medical Affairs
John Weet, PhD, Vice President, Worldwide Regulatory Affairs
Ronald Trust, PhD, Executive Director, Regulatory Affairs, North America
Briton Shell, PhD, Director, Regulatory Affairs, North America
Angela Birchler, PhD, Executive Director, CMC and Manufacturing
Roger Keding, PhD, Vice President of Manufacturing
Dennis Casey, PhD, CMC and Pharmaceutical Sciences

INTRODUCTION

After introductions, the Clinical Team Leader conveyed the following information:

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may or may not be able to consider your response before we take an action on your application during this review cycle.

1. Significant Review Issues:

None to report at this time.

2. Information Requests:

Nothing pending at this time. There may be future information requests as the review cycle continues.

3. Major Safety Concerns:

Liver function test elevations were observed at a higher frequency in the dalbavancin as compared to comparator arm. Hepatic effects of dalbavancin are still being reviewed, but will likely be addressed with labeling changes.

4. Risk Management Update:

At this time, the Office of New Drugs and the Office of Surveillance and Epidemiology have not conclusively determined whether a risk evaluation and mitigation strategy (REMS) will be necessary to ensure that the benefits of the drug outweigh the risks. However, based on the information currently available, we do not believe that a REMS will be necessary. A final determination on the need for a REMS will be made during the review of your application.

5. Advisory Committee Meeting Plans:

NDA 21-883 will be taken to Advisory Committee on the afternoon of March 31, 2014. Please continue to work with Jennifer Shepard, RPh, Designated Federal Officer with the Anti-Infective Drugs Advisory Committee Staff for specific details regarding deliverables and due dates.

6. Proposed Date for Late-Cycle Meeting/Other Projected Milestones:

- **February 28, 2014:** *The Division will be conveying preliminary, proposed revisions to the product labeling to you electronically.*

Be advised that these revisions may be limited to a certain section (or sections) of the label in stepwise fashion, as reviews are ongoing and the outcome of the Advisory Committee Meeting may necessitate additional labeling discussions. In addition, we will communicate with you regarding any preliminary assessment(s) as to whether or not there will be post marketing commitments (PMC) and/or requirements (PMR).

- **March 17, 2014:** *This will be the date of your Late Cycle Review Meeting. You may elect to have this meeting by teleconference or in person with the review team at the White Oak Campus. We will provide a briefing document for this meeting to you electronically on or about March 3, 2014. Topics of discussion at the meeting include, but are not limited to substantive review issues, additional applicant data (e.g., to be submitted in response to any pending information request or at the Sponsor's discretion), REMS or other risk management actions, potential PMRs/PMCs and major labeling issues (if applicable).*
- **May 26, 2014:** *DAIP will take an action on your application.*

CONCLUSION:

The Sponsor confirmed with the Division that the information conveyed would be documented in meeting minutes. They also requested a list of attendees.

There were no further questions/clarifications and the teleconference ended amicably.

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/s/

MAUREEN P DILLON PARKER
01/16/2014



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 021883

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Durata Therapeutics, Inc.
322 East Main Street
Branford, CT 06405

ATTENTION: Briton Shell, PhD
Director, Regulatory Affairs, North America

Dear Dr. Shell:

Please refer to your New Drug Application (NDA) resubmission, dated September 25, 2013, and received September 26, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Dalbavancin Hydrochloride for Injection, 500 mg per vial.

We also refer to your correspondence, dated and received November 8, 2013, requesting review of your proposed proprietary name, Dalvance. We have completed our review of the proposed proprietary name and have concluded that it is acceptable.

If **any** of the proposed product characteristics as stated in your November 8, 2013, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Karen Townsend, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-5413. For any other information regarding this application contact Christopher Davi at (301) 796-0702 the Office of New Drugs (OND) Regulatory Project Manager.

Sincerely,

{See appended electronic signature page}

Kellie A. Taylor, Pharm.D., MPH
Deputy Director
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

KELLIE A TAYLOR
11/26/2013



NDA 21-883

Pfizer Global Pharmaceuticals, Inc.
Attention: Elina Surlevitch-Chin, PhD
Director, Regulatory Affairs
235 East 42nd Street
New York, NY 10017

Dear Dr. Chin:

Please refer to your New Drug Application (NDA) for dalbavancin. We also refer to the meeting between representatives of your firm and the FDA on September 23, 2008. The purpose of the meeting was to discuss some of the aspects surrounding the withdrawal of NDA 21-883.

The official minutes of that meeting are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call J. Christopher Davi, MS, at (301) 796-0702.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Acting Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosures: Minutes from meeting



MEMORANDUM OF TELECONFERENCE

MEETING DATE: September 23, 2008
MEETING TIME: 8:30 to 9:00 AM, EST

APPLICATION (DRUG): NDA 21-883 (dalbavancin)
SPONSOR:

MEETING CHAIR: Wiley A. Chambers, MD, Acting Division Director, Division of Anti-Infective and Ophthalmology Products (DAIOP)

MEETING RECORDER: J. Christopher Davi, MS, Regulatory Project Manager

FDA PARTICIPANTS (DAIOP):
Wiley Chambers, MD, Acting Division Director
Katherine A. Laessig, MD, Deputy Division Director
Sumathi Nambiar, MD, MPH, Acting Deputy Division Director for Safety
Janice K. Pohlman, MD, MPH, Acting Medical Team Leader
J. Christopher Davi, MS, Regulatory Project Manager

INDUSTRY PARTICIPANTS (Pfizer, Inc.):
Elina Surlevitch-Chin, PhD, Director, Regulatory Affairs
Michael Dunn, MD, Therapeutic Head, Infectious Disease

MEETING OBJECTIVE:

To discuss the Sponsor's decision to withdraw NDA 21-883.

DISCUSSION POINTS:

- The Sponsor notified the Agency that they had elected to withdraw NDA 21-883 for various reasons, [REDACTED] (b) (4)
- [REDACTED] (b) (4)
- The Division acknowledged this, but reminded the Sponsor that the action letter instructs the Sponsor to call if they have any questions regarding the action. The Sponsor acknowledged this.

Minutes Prepared by: *{See appended electronic signature page}*
J. Christopher Davi, MS
Regulatory Project Manager

Concurrence by: *{See appended electronic signature page}*
Wiley A. Chambers, M.D.
Deputy Division Director

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/s/

Christopher Davi
11/12/2008 02:24:32 PM
CSO

Wiley Chambers
11/19/2008 11:35:30 PM
MEDICAL OFFICER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-883

Pfizer Global Pharmaceuticals
Attention: Nadia Kirzecky
Liaison Director, Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017

Dear Dr. Kirzecky:

We have received your September 15, 2008 correspondence on September 15, 2008 notifying us that you are withdrawing your unapproved new drug application (NDA) for dalbavancin for injection (b)(4) 500 mg. This application was filed on February 18, 2005.

In accordance with 21 CFR 314.65, this application is withdrawn as of September 15, 2008. If you decide to resubmit this application, this withdrawal will not prejudice any future decisions on filing. You may reference information contained in this withdrawn application in any resubmission. However, because we retain only the archival copy of a withdrawn application in our files, you should resubmit appropriate review copies of all information. Retain the above NDA number for the resubmitted application.

In addition, the resubmitted application should address the following deficiencies identified during our preliminary review of the withdrawn application:

- Your proposed label should be submitted in Physician's Labeling Rule (PLR) format.
- A response to the Agency's information request of August 25, 2008 regarding the patient population in Study 08.
- A response to the Agency's inquiries of September 8, 2008 regarding your proposed pediatric drug development plan.

If you have any questions, call J. Christopher Davi, Regulatory Health Project Manager, at (301) 796-0702.

Sincerely,

{See appended electronic signature page}

Katherine A. Laessig, MD
Deputy Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

Kathrine Laessig
9/16/2008 03:37:07 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-883

Vicuron Pharmaceuticals, Inc., a subsidiary of Pfizer
c/o Pfizer Inc.
Attention: Ms. Nadia Kirzecky
Regulatory Lead
235 East 42nd Street
New York, NY 10017

Dear Ms. Kirzecky:

Please refer to your New Drug Application (NDA) for dalbavancin. We also refer to the teleconference between representatives of your firm and the FDA on May 14, 2008. The purpose of the teleconference was to discuss issues surrounding the justification of non-inferiority margins for your pivotal studies.

The official minutes of that teleconference are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call J. Christopher Davi, MS, at (301) 796-0702.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Acting Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosures: Minutes from teleconference



MEMORANDUM OF TELECONFERENCE

DATE: May 14, 2008
TIME: 4:00 to 5:00 PM, EST

APPLICATION (DRUG): NDA 21-883 (dalbavancin powder for injection)

SPONSOR: Vicuron Pharmaceuticals, Inc., a subsidiary of Pfizer

TYPE OF MEETING: Teleconference

MEETING CHAIR: Wiley A. Chambers, MD, Acting Director, Division of Anti-Infective and Ophthalmology Products (DAIOP)

MEETING RECORDER: J. Christopher Davi, MS, Regulatory Project Manager

FDA PARTICIPANTS (DAIOP):

Wiley Chambers, MD, Acting Division Director
Sumathi Nambiar, MD, MPH, Medical Team Leader
Janice K. Pohlman, MD, MPH, Medical Reviewer
Thamban Valappil, PhD, Team Leader, Biometrics
Scott Komo, DrPh, Biometrics Reviewer
Frederic J. Marsik, PhD, Clinical Microbiology Team Leader
J. Christopher Davi, MS, Regulatory Project Manager

INDUSTRY PARTICIPANTS (Vicuron Pharmaceuticals, Inc., a subsidiary of Pfizer):

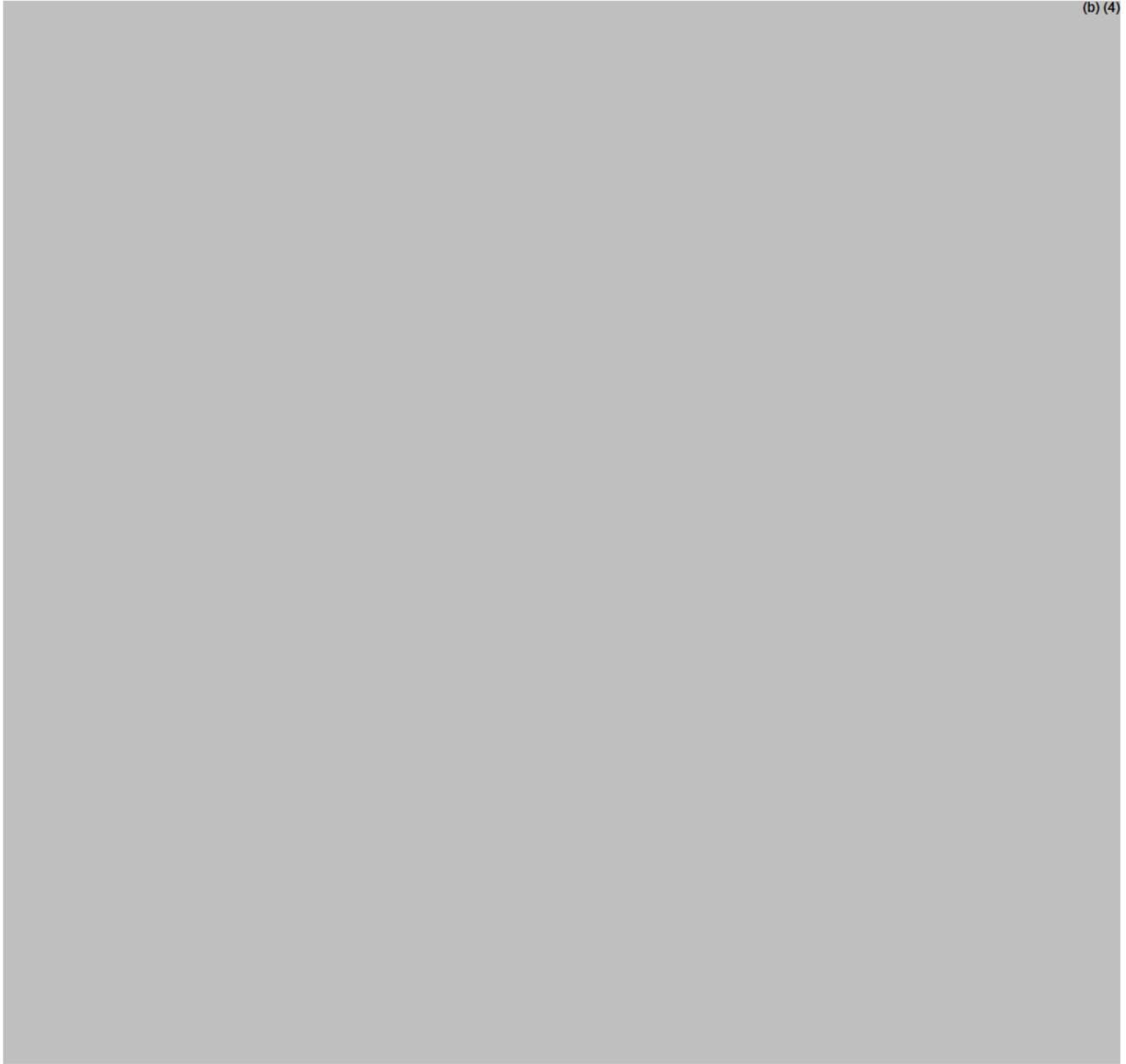
Deborah Kirby, MD, Development Team Leader, Antibacterials
Sailaja Puttagunta, MD, Clinician
Daniel Meyer, Statistics Head, Infectious Diseases
Elina Srulevitch-Chin, Regulatory Therapeutic Area Head, Infectious Diseases
Nadia Kirzecky, Regulatory Lead

MEETING OBJECTIVE:

- To discuss issues surrounding the justification of non-inferiority margins for pivotal studies VER001-8 and VER001-9.

SUMMARY OF DISCUSSION:

The Division of Anti-Infective and Ophthalmology Products (DAIOP) and Vicuron held a teleconference to discuss the above referenced objective. DAIOP provided preliminary comments to the Sponsor on May 12, 2008 (appended). Vicuron presented a short slide presentation. Discussion points generated from the preliminary comments are provided in bullet format as follows:



(b) (4)

Minutes Prepared by: *{See appended electronic signature page}*
J. Christopher Davi, MS
Regulatory Project Manager

Concurrence by: *{See appended electronic signature page}*
Wiley A. Chambers, M.D.
Acting Division Director

Dear Ms. Kirzecky:

In anticipation of our teleconference on May 14, 2008, please see the attached responses from the Agency (*italics*) with regard to the questions posed in your briefing document dated April 25, 2008 (NDA 21-883):

1. Does the information provided by the Sponsor [REDACTED] (b) (4)

(b) (4)

Division response: No. [REDACTED] (b) (4)

2. [REDACTED] (b) (4)

Division response: Yes, if combined with additional supporting information requested in question #1 above.

3. Does the Agency agree that the information provided in this document would constitute as a response to the clinical outstanding issue listed in the approvable letter dated 20 December 2007?

Division response: The approach outlined in #2 above would constitute a response to deficiency #3 included in the December 20, 2007 approvable letter. It should be noted that there were additional issues in the action letter.

We look forward to our discussion on May 14, 2008. If you have question in the interim, please contact me at (301) 796-0702.

J. Christopher Davi, MS
Regulatory Project Manager
Division of Anti-Infective and Ophthalmology Products

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/s/

Wiley Chambers
8/5/2008 10:56:29 PM

Davi, Christopher

From: Bonapace, Charles
Sent: Wednesday, May 17, 2006 3:24 PM
To: Davi, Christopher
Cc: Soreth, Janice M; Jarugula, Venkateswar
Subject: (b) (4)

Chris,

The clin pharm team is in agreement with the Clinical Pharmacology and (b) (4) submitted with the complete response to action letter dated March 24, 2006. Feel free to inform the sponsor that we are in agreement with these sections and will not be recommending any changes.

Chuck



NDA 21-883

Vicuron Pharmaceuticals, Inc.
Attention: Eve Damiano
Vice President, Regulatory Affairs
455 South Gulph Road
King of Prussia, PA 19406

Dear Ms. Damiano:

Please refer to your New Drug Application (NDA) dated December 21, 2004, received December 21, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Dalbavancin powder for injection, (b)(4) 500 mg.

We also refer to the Agency's action letter dated September 21, 2005, in which you were notified that the review of your application had been completed, and that the application was approvable, contingent upon the resolution of two (2) deficiencies (i.e., isolated intermediate storage and labeling). In addition to the two deficiencies enumerated in the approvable letter, the Division wishes to provide recommendations and comments on several noteworthy items identified during the review. These additional noteworthy items are listed below; some of these items were discussed during the review of NDA 21-883. We encourage you to address these items as part of your ongoing development plan for dalbavancin:

Under 21 CFR 314.102(d), you may request an informal meeting or telephone conference with the Division of Anti-Infective and Ophthalmology Products to further discuss the items in this advice letter.

CHEMISTRY, MANUFACTURING AND CONTROLS:

1. We remind you of your commitments in the amendment dated September 9, 2005 (b)(4)

[Redacted]

2. Concerns remain regarding the specificity of the regulatory HPLC assays, as peak purity was demonstrated only by (b)(4). A method with greater specificity such as LC-MS should be provided. Please provide for additional drug substance and drug product samples to be sent to the following individual at our St. Louis lab:

Lucinda Buhse, Ph.D. (Lucinda.Buhse@fda.gov)
FDA, HFD-920
1114 Market St. Room 1002
St. Louis, Mo. 63101
314-539-2134

CLINICAL:

As hypoglycemia and hyperglycemia were observed more commonly in dalbavancin-treated patients during the clinical trials, a study designed to explore the effect of dalbavancin administration on glucose homeostasis and relationship of serum glucose levels to dalbavancin pharmacokinetic parameters in both diabetic and non-diabetic patients is recommended. This could be performed in conjunction with an efficacy trial in the treatment of infected ulcers and other deep soft tissue infections.

MICROBIOLOGY:

Additional information on the anaerobic susceptibility testing method for Dalbavancin (to include reproducibility, accuracy, and the role of polysorbate 80) needs to be provided prior to the Agency's consideration of including any anaerobic bacteria in the package insert.

If you have any questions, call J. Christopher Davi, Regulatory Health Project Manager, at (301) 796-0702.

Sincerely,

{See appended electronic signature page}

Janice M. Soreth, M.D.
Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

Janice Soreth
10/4/2005 12:18:12 PM

LATE-CYCLE COMMUNICATION
DOCUMENTS



NDA 21-883

LATE-CYCLE MEETING MINUTES

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

Dear Dr. Shell:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) for Dalvance (dalbavancin hydrochloride) Lyophilized Powder for Injection, 500 mg.

We also refer to the Late-Cycle Meeting (LCM) teleconference between representatives of your firm and the FDA on March 20, 2014.

A copy of the official minutes of the LCM is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call J. Christopher Davi, Senior Regulatory Project Manager at (301) 796-0702.

Sincerely,

{See appended electronic signature page}

John J. Alexander, MD, MPH
Medical Team Leader
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Late Cycle Meeting Minutes



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF LATE-CYCLE TELECONFERENCE

Meeting Date and Time: March 20, 2014
Application Number: NDA 21-883
Product Name: Dalvance (dalbavancin hydrochloride)
Applicant Name: Durata Therapeutics International, B.V.

Meeting Chair: John J. Alexander, MD, MPH
Meeting Recorder: J. Christopher Davi, MS

FDA ATTENDEES]

Edward M. Cox, MD, MPH, Director, OAP
John Farley, MD, MPH, Deputy Director, OAP
Sumathi Nambiar, MD, MPH, Director, DAIP
Katherine A. Laessig, MD, Deputy Director, DAIP
Joseph Toerner, MD, Acting Deputy Director for Safety
John Alexander, MD, MPH, Medical Team Leader
Dmitri Iarikov, MD PhD, Medical Reviewer
John Lazor, Pharm D, Director, Office of Clinical Pharmacology
Ryan Owen, PhD, Clinical Pharmacology Reviewer
Yang He, PhD, Clinical Pharmacology Reviewer
Terry Miller, PhD, Nonclinical Pharmacology Reviewer
Thamban Valappil, PhD, Biostatistics Team Leader
Chris Kadoorie, PhD, Biostatistics Reviewer
Kerry Snow, MS, Clinical Microbiology Team Leader
Peter Coderre, PhD, MBA, Clinical Microbiology Reviewer
Steven Hertz, Consumer Safety Officer, Compliance
Mark Seggel, PhD, CMC Reviewer
David L. Roeder, MS, Associate Director of Regulatory Affairs, OAP
Diem-Kieu Ngo, CDR Senior Supervisor, Advisory and Consultants Staff
Jennifer Shepherd, RPh, LCDR, Advisory and Consultants Staff
Maureen Dillon-Parker, Chief, Project Management Staff
J. Christopher Davi, MS, Senior Regulatory Project Manager
Mona Atkinson, MS, MBA, Regulatory Project Manager

EASTERN RESEARCH GROUP ATTENDEES

(b) (6)

APPLICANT ATTENDEES

Michael Dunne, MD, Chief Medical Officer

James Baldassarre, MD, Executive Director of Clinical and Medical Affairs

John Weet, PhD, Vice President, Worldwide Regulatory Affairs

Ronald Trust, PhD, Executive Director, Regulatory Affairs, North America

Briton Shell, PhD, Director, Regulatory Affairs, North America

1.0 BACKGROUND

NDA 21-883 was submitted on September 26, 2013, for Dalvance (dalbavancin hydrochloride) for injection, 500 mg for the proposed indication of Acute Bacterial Skin and Skin Structure Infections (ABSSSI). The application has a PDUFA goal date of May 26, 2014.

FDA issued a Background Package to Durata in preparation for this meeting on March 12, 2014.

2.0 DISCUSSION

- **Introductory Comments:** Dr. Alexander began the discussion with the following introductory comments:

The purpose of a LCM is to share information and to discuss any substantive review issues that we have identified to date, Advisory Committee (AC) meeting plans and our objectives for the remainder of the review. The application has not yet been fully reviewed by the signatory authority, Division Director, and Cross-Discipline Team Leader (CDTL) and therefore, the meeting will not address the final regulatory decision for the application. We are sharing this material to promote a collaborative and successful discussion at the meeting. During the meeting, we may discuss additional information that may be needed to address the identified issues and whether it would be expected to trigger an extension of the PDUFA goal date if the review team should decide, upon receipt of the information, to review it during the current review cycle. If you submit any new information in response to the issues identified in this background package prior to this LCM or the AC meeting, we may not be prepared to discuss that new information at this meeting.

- **Substantive Review Issues:**

- **Hepatotoxicity:** The Sponsor opened the discussion by indicating that they understood the Division's concerns around hepatotoxicity. However, the Sponsor believed that this may be due to a discrepancy between Treatment Emergent Adverse Events (TEAE) and Adverse Events (AE). The Sponsor indicated that some of the adverse events may be pre-existing (e.g., elevated Liver Function Tests (LFTs)) among all comers.

The Sponsor added that there were also a significant number of patients with elevated LFTs at baseline and that they felt this was an important point to make at the Advisory Committee Meeting. The Sponsor did not believe there was a significant safety signal with LFTs, depending upon the analysis.

The Division acknowledged the Sponsor's points, but believed that there were imbalances with LFT abnormalities (i.e., dalbavancin versus comparator). The Division would be interested in the analyses that would substantiate the Sponsor's position. The Sponsor agreed to provide additional information.

(b) (4)

- **Susceptibility Test Interpretive Criteria:** The Division informed the Sponsor that the interpretive criteria may have to be revised and that this determination will involve a multidisciplinary review. The Sponsor indicated that the interpretive criteria have been historically the same through the drug development process. The Sponsor added that Study 009 did not provide much information in support of the interpretive criteria. In addition, some microbiology methodology can cause issues with interpretive criteria (e.g., dalbavancin's binding to plastic). This is not an issue *in vivo*.

The Division acknowledged this point and added that the Sponsor had done a significant amount of work to develop *in vitro* susceptibility test methods. The Division also noted that there was a disc susceptibility issue.

- **Compliance Update:** The Sponsor was informed that the manufacturing inspection of the (b) (4) manufacturing facility had been completed in (b) (4). The Sponsor was encouraged to contact (b) (4) regarding the results of the inspection. The Sponsor was informed that other inspections are scheduled and that results are pending.

- **Hemorrhage as an AE:** The Sponsor indicated that many patients had the AE before receiving dalbavancin and that they (Sponsor) have case report forms that will elucidate more information on this. The Sponsor added that the distinction between AEs and TEAEs has implications for the AE analyses related to hemorrhage, as well as for hepatotoxicity analyses. The Division expressed interest in seeing any additional data to this effect. The Division cited a non-clinical study report (i.e., Rabbit Platelet Study) in which dalbavancin was found to have an inhibitory effect on coagulation. The Division added that additional consideration of Hemorrhage as an AE can be held during future labeling discussions.

3.0 ADVISORY COMMITTEE MEETING

The Sponsor indicated that they do not want to focus on the Hemorrhage as an AE discussion at the AC meeting. The Sponsor asked for guidance as to what will be presented by the Division at the AC. The Division indicated that the current policy does not allow them to provide the Agency's slides to the Sponsor prior to the AC. The Division stated that the development of endpoints for ABSSSI trials will be discussed before the Sponsor's presentation.

4.0 POSTMARKETING REQUIREMENTS

There will be a pediatric study requirement for dalbavancin; the pediatric plan will be discussed at an upcoming Pediatric Review Committee (PeRC) meeting. In addition, the Division informed the Sponsor that there would likely be a PMR (i.e., microbiology surveillance study) to monitor for dalbavancin resistance.

This application has not yet been fully reviewed by the signatory authority, Division Director, and Cross-Discipline Team Leader (CDTL); therefore, as outlined at the start of the discussion, this meeting did not address the final regulatory decision for the application.

-End

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/s/

JOHN J ALEXANDER
04/13/2014