

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
050824Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 50-824

SUPPL #

HFD # 590

Trade Name None

Generic Name Omeprazole 20 mg capsules/clarithromycin 500 mg tablets/amoxicillin 500 mg capsules

Applicant Name DAVA Pharmaceuticals

Approval Date, If Known February 8, 2011

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 NO

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

505(b)(2)

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 NO

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.

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:

d) Did the applicant request exclusivity?

YES NO

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

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

YES 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?

NO

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?

YES 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.

YES 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.)

YES NO

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

NDA# 19-810 Prilosec (omeprazole)

NDA# 50-662 Biaxin (clarithromycin)

NDA# 50-459 Amoxil (amoxicillin)
62-216 Amoxicillin

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:
Title:
Date:

Name of Office/Division Director signing form:
Title:

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

JUDIT R MILSTEIN
02/08/2011

RENATA ALBRECHT
02/08/2011
Exclusivity Summary

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 50-824	NDA Supplement # N/A	If NDA, Efficacy Supplement Type:
Proprietary Name: None Established/Proper Name: Omeprazole delayed release capsules, clarithromycin tablets and amoxicillin capsules Dosage Form: Omeprazole delayed release capsules, 20 mg, clarithromycin tablets, 500 mg, and amoxicillin capsules, 500 mg		Applicant: DAVA Pharmaceuticals Agent for Applicant (if applicable):
RPM: Judit Milstein		Division: Division of Special Pathogen and Transplant Products
<p>NDA: NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>	<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)):</p> <p>Prilosec (omeprazole), NDA 19-810</p> <p>Biaxin (clarithromycin), NDA 50-662</p> <p>Amoxil (amoxicillin), NDA 50-459/ANDA 62-216</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>This product provides for the co-packaging of the three above listed products</p> <p><input type="checkbox"/> If no listed drug, check box and explain:</p> <p><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input checked="" type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check: February 8, 2011</p> <p>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.</p>	
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>February 8, 2011</u> 		<input checked="" type="checkbox"/> 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>) 		<input checked="" type="checkbox"/> CR July 20, 2010

¹ The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

<p>❖ If accelerated approval, were promotional materials received? Note: For accelerated approval (21 CFR 314.510/601.41), 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 _____</p>	<input checked="" type="checkbox"/> N/A
<p>❖ Application Characteristics²</p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): 4</p> <p> <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC </p> <p> NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies </p> <p> BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies </p> <p> <input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request </p> <p>Comments:</p>	
<p>❖ BLAs only: <i>RMS-BLA Product Information Sheet for TBP</i> has been completed and forwarded to OBPS/DRM (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes, date
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> Press Office notified of action (by OEP) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	<input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

² 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.

❖ Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/>
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) <input checked="" type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<input checked="" type="checkbox"/> No paragraph III certification Date patent will expire
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i> 	<input type="checkbox"/> N/A (no paragraph IV certification) <input checked="" type="checkbox"/> Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for **each** paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "Yes," skip to question (4) below. If "No," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If "No," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (5).

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
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CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ³	Yes
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>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) AP February 8, 2011 CR July 20, 2010
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	X (labeling submitted February 7, 2011)
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	September 21, 2009
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	N/A

³ Fill in blanks with dates of reviews, letters, etc.
Version: 5/14/10

<ul style="list-style-type: none"> ❖ Medication Guide/Patient Package Insert/Instructions for Use (<i>write submission/communication date at upper right of first page of each piece</i>) 	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	
<ul style="list-style-type: none"> ❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>) 	
<ul style="list-style-type: none"> • Most-recent draft labeling 	X- Submitted February 7, 2011
<ul style="list-style-type: none"> ❖ Proprietary Name <ul style="list-style-type: none"> • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) 	February 8, 2011 (memo, name not acceptable) July 14, 2010 (Acknowledgment of WD of tradename) March 2, 2010 (Proprietary name denied) December 8, 2009 Reviews: January 21, 2011 March 2, 2010
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input type="checkbox"/> RPM <input checked="" type="checkbox"/> DMEPA July 13, 2010 <input type="checkbox"/> DRISK <input checked="" type="checkbox"/> DDMAC July 1, 2010 Consult to DDMAC January 15, 2010 <input type="checkbox"/> CSS <input checked="" type="checkbox"/> Other reviews Review from DGP-February 7, 2011 Consult to DGP-August 17, 2010 SEALD: December 14, 2010 Review from PMHS-June 2, 2010 Consult to PMHS-April 23, 2010.
Administrative / Regulatory Documents	
<ul style="list-style-type: none"> ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) 	September 16, 2009
<ul style="list-style-type: none"> ❖ 505(b)(2) Assessment (<i>indicate date</i>) 	February 8, 2011
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) 	<input checked="" type="checkbox"/> Included

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
Version: 5/14/10

<ul style="list-style-type: none"> ❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm 	
<ul style="list-style-type: none"> • Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<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>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC January 26, 2011 If PeRC review not necessary, explain: _____ • Pediatric Page (<i>approvals only, must be reviewed by PERC before finalized</i>) 	Copy of document presented at PeRC included-February 8, 2011 <input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>) 	<input checked="" type="checkbox"/> Verified, statement is acceptable
<ul style="list-style-type: none"> ❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>) 	ACK letter January 5, 2011 Fax July 6, 2010 Fax June 3, 2010 Letter May 11, 2010-Pediatric waiver denied Filing Communication December 4, 2009 Fax November 17, 2009 IR letter October 28, 2009 Fax October 26, 2009 ACK October 7, 2009 ACK withdrawal September 23, 2009 IR letter September 16, 2009 Meeting Minutes September 15, 2009 ACK letter July 23, 2009
<ul style="list-style-type: none"> ❖ Internal memoranda, telecons, etc. 	N/A
<ul style="list-style-type: none"> ❖ Minutes of Meetings 	
<ul style="list-style-type: none"> • Regulatory Briefing (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> • If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> N/A or no mtg
<ul style="list-style-type: none"> • Pre-NDA/BLA meeting (<i>indicate date of mtg</i>) 	Minutes of the preNDA meeting (PIND 101174)- March 18, 2008
<ul style="list-style-type: none"> • EOP2 meeting (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> • Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>) 	N/A
<ul style="list-style-type: none"> ❖ Advisory Committee Meeting(s) 	<input checked="" type="checkbox"/> No AC meeting
<ul style="list-style-type: none"> • Date(s) of Meeting(s) 	
<ul style="list-style-type: none"> • 48-hour alert or minutes, if available (<i>do not include transcript</i>) 	

Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	AP Action February 8, 2011 CR Action July 20, 2010
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	AP Action February 8, 2011 CR Action July 19, 2010
PMR/PMC Development Templates (<i>indicate total number</i>)	<input checked="" type="checkbox"/> None
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	N/A
• Clinical review(s) (<i>indicate date for each review</i>)	See CDTL Review dated February 8, 2011 Filing review October 14, 2009 Filing review August 3, 2009
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input checked="" type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	X-This is a 505(b)(2) application and no new clinical studies were submitted. See CDTL Review dated February 8, 2011, item 9.0 FINANCIAL DISCLOSURE
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management <ul style="list-style-type: none"> • REMS Documents and Supporting Statement (<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>) 	<input checked="" type="checkbox"/> None
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	January 10, 2011 June 30, 2010 Filing review July 23, 2009
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Review(s) (<i>indicate date for each review</i>)	February 7, 2011 July 16, 2010 Filing review August 19, 2009

⁵ Filing reviews should be filed with the discipline reviews.
Version: 5/14/10

Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) <i>(indicate date for each review)</i>	February 8, 2011 July 16, 2010 Filing review August 18, 2009
❖ DSI Clinical Pharmacology Inspection Review Summary <i>(include copies of DSI letters)</i>	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Supervisory Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>	February 7, 2011 July 19, 2010 Filing review August 18, 2009
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> No
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None
❖ DSI Nonclinical Inspection Review Summary <i>(include copies of DSI letters)</i>	<input checked="" type="checkbox"/> 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>	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>	February 7, 2011 July 16, 2010 July 8, 2010 Filing review August 19, 2009
❖ Microbiology Reviews <input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i> <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> Not needed
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>	See Product Quality review dated July 8, 2010, page 30.
<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>	See Product Quality filing review dated August 19, 2009

❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) <i>(date completed must be within 2 years of action date)</i>	Date completed: July 7, 2011 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
<input type="checkbox"/> BLAs: TB-EER <i>(date of most recent TB-EER must be within 30 days of action date)</i>	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation <i>(check box only, do not include documents)</i>	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed

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/s/

JUDIT R MILSTEIN
02/10/2011
Action package checklist



NDA 50-824

**ACKNOWLEDGE --
CLASS 1 COMPLETE RESPONSE**

DAVA Pharmaceuticals, Inc.
Attention: Susan Hamet
Vice President, Regulatory Affairs
Parker Plaza
400 Kelby Street, 10th Floor
Fort Lee, NJ 07024

Dear Ms. Hamet:

We acknowledge receipt on December 8, 2010, of your December 7, 2010, resubmission to your new drug application pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Omeprazole Delayed-Release Capsules, 20 mg/Clarithromycin Tablets, 500 mg/Amoxicillin Capsules, 500 mg.

We consider this a complete, class 1 response to our July 20, 2010, action letter. Therefore, the user fee goal date is February 8, 2011.

If you have any questions, call me at 310-796-0763.

Sincerely,

{See appended electronic signature page}

Judit Milstein
Chief, Project Management Staff
Division of Special Pathogen and Transplant
Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

JUDIT R MILSTEIN

01/05/2011

Acknowledgment of Class I resubmission

MEMORANDUM

To: Judit Milstein
Division of Special Pathogen and Transplant Products

From: Iris Masucci, PharmD, BCPS, Office of Medical Policy
for the Study Endpoints and Label Development (SEALD) Team, OND

Date: June 7, 2010

Re: Comments on draft labeling for TTBN
(omeprazole/clarithromycin/amoxicillin)
NDA 50-824

We have reviewed the proposed label for TTBN (FDA version received 6/1/10) and offer the following comments. These comments are based on Title 21 of the Code of Federal Regulations (201.56 and 201.57), the preamble to the Final Rule, labeling Guidances, and FDA recommendations to provide for labeling quality and consistency across review divisions. We recognize that final labeling decisions rest with the review division after a full review of the submitted data.

Please see attached label for recommended changes. Note that the Clinical Studies section was not reviewed because it was yet to be completed by the Division.

30 Page(s) of Draft Labeling have been Withheld in Full as
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/s/

IRIS P MASUCCI
11/19/2010

LAURIE B BURKE
12/14/2010

REQUEST FOR CONSULTATION

TO (Office/Division): *Wes Ishihara*
LT, U.S. Public Health Service Commissioned Corps
Chief, Project Management Staff
Division of Gastroenterology Products
Office of Drug Evaluation III
CDER/FDA

FROM (Name, Office/Division, and Phone Number of Requestor): *Renata Albrecht, MD, Division of Special Pathogen and Transplant Products, Office of Antimicrobial Products*

DATE
8-17-2010

IND NO.

NDA NO.
(b) (4)
NDA 50-824

TYPE OF DOCUMENT
Labeling Review

DATE OF DOCUMENT

NAME OF DRUG
(b) (4)

PRIORITY
CONSIDERATION
Medium

CLASSIFICATION OF DRUG
Treatment of H. pylori

DESIRED COMPLETION DATE
10/18/2010

Omeprazole/clarithromycin/amoxicillin

NAME OF FIRM: N/A

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input checked="" type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS:

(b) (4)

NDA 50-824, (no proprietary name found acceptable to date by OSE) was submitted on September 22, 2009, and received a CR letter (July 20, 2010), which also included requested revisions to the labeling in PLR format. Both products are intended for the "Treatment of H.Pylori infections" as triple combinations. Given that these products are co-packages, the final labeling parallels the labeling of the individual drugs. However, in updating the labeling information for these products, our reviewers have proposed some revisions in formatting,

specifically to include subheadings within Sections to facilitate the location of the information. They have also rearranged the text to fit within these subheadings, and updated the language to be consistent with the recommendations from SEALD and Maternal Health Guidance.

We request that you review the sections/text of the package inserts as they refer to [REDACTED] (b) (4) [REDACTED] omeprazole products and/or whether the proposed variations in content and format are acceptable. We remind you that both Prevpac and NDA 50-824 are exclusively intended for the treatment of H. pylori infections.

[REDACTED] (b) (4)

Project Manager: Judit Milstein (6-0763)

Medical Officer: Joette Meyer (6-1600)

Attachments: [REDACTED] (b) (4) [REDACTED]
NDA 50-824- Division's proposed labeling in PLR format, included in the CR letter

SIGNATURE OF REQUESTOR Judit Milstein, Chief Project Management Staff	METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DARRTS <input type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

40 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA (b) (4)

(b) (4)

(b) (4)

(b) (4)

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/s/

OZLEM A BELEN
07/29/2010

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(CCI/TS) immediately following this page

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-50824

ORIG-1

DAVA
PHARMACEUTICA
LS INC

OMEPRAZOLE
25MG/AMOXOCILLIN
500MG/CLARITHROMYCIN
500MG

(b) (4)

(b) (4)

(b) (4)

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/s/

JUDIT R MILSTEIN

08/17/2010

Consult to DGP (b) (4) /omeprazole labeling for H pylori products



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Antimicrobial Products

FACSIMILE TRANSMITTAL SHEET

DATE: July 6, 2010

To: Susan Hamet, Vice President Regulatory Affairs	From: Judit Milstein, Chief Project Management Staff
Company: DAVA Pharmaceuticals	Division of Special Pathogen and Transplant Products
Fax Number: 201-592-4640	Fax Number: 301-796-9881
Phone Number: 201-592-4476	Phone Number: 301-796-1600

Subject: Preliminary comments on Labels and Labeling

Total no. of pages including cover: 9

Document to be mailed: YES NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

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If you have any questions regarding the contents of this transmission, please contact me at 301-796-1600.

Judit Milstein
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

NDA 50-824
Compliance Pack for Omeprazole/clarithromycin/amoxicillin
DAVA Pharmaceuticals

RE: Comments on Labels and Labeling

Dear Dr. Hamet,

We refer to your NDA submission dated September 21, 2009, received September 22, 2009 for the co-packaging of omeprazole, clarithromycin and amoxicillin.

Find enclosed the Division's preliminary comments for the Labels and Labeling.

A. General Comments for All Labels and Labeling

1. Ensure that the active ingredients are listed as omeprazole/clarithromycin/amoxicillin across all product labels and labeling (As currently presented, the insert labeling lists ^{(b) (4)} However, the daily administration card lists the active ingredients in two ways: omeprazole/amoxicillin/clarithromycin and omeprazole/clarithromycin/amoxicillin. The carton labeling lists omeprazole/clarithromycin/amoxicillin).
2. Please submit revised labels and labeling reflecting the approved proprietary name for this product along with all associated graphics and logos, when available, for our review.

B. Container Labels: Patient Card Front (Trade and Sample)

3. ^{(b) (4)}
4. Move the Trademark to be immediately above the established names, and remove the additional Omeprazole-Amoxicillin-Clarithromycin (See attached FDA mock-up revisions)
5. Change the presentation of the active ingredients to include the strength immediately after the established name as follows:
Omeprazole Delayed Release Capsules, USP, 20 mg
Clarithromycin Tablets, USP, 500 mg
Amoxicillin Capsules, USP, 500 mg

6. Use the numbers provided in the description of the active ingredients at the top of the dosage card (e.g. 1,2,3) to identify the actual corresponding capsules/tablets at the bottom of the card, [REDACTED] (b) (4) [REDACTED].
7. Increase the prominence of the graphics representing the morning and evening doses to provide better differentiation, [REDACTED] (b) (4) [REDACTED].

C. Container Labels: Blister Mat (Trade and Sample)



Please, let me know if you have any questions regarding this request.

Judit Milstein
Chief, Project Management Staff
Division of Special Pathogen and Transplant Products
301-796-0763

4 Page(s) of Draft Labeling have been Withheld in Full as
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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	ORIG-1	DAVA PHARMACEUTICA LS INC	OMEPRAZOLE 25MG/AMOXOCILLIN 500MG/CLARITHROMYCIN 500MG

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/s/

JUDIT R MILSTEIN

07/06/2010

Comments on labels and labeling



Food and Drug Administration
 Center for Drug Evaluation and Research
 Office of Antimicrobial Products

FACSIMILE TRANSMITTAL SHEET

DATE: June 3, 2010

To: Susan Hamet, Vice President Regulatory Affairs	From: Judit Milstein, Chief Project Management Staff
Company: DAVA Pharmaceuticals	Division of Special Pathogen and Transplant Products
Fax Number: 201-592-4640	Fax Number: 301-796-9881
Phone Number: 201-592-4476	Phone Number: 301-796-1600

Subject: Request for revisions to the carton package, and physical samples of the carton and blister card

Total no. of pages including cover: 3

Document to be mailed: YES NO

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If you have any questions regarding the contents of this transmission, please contact me at 301-796-1600.

Judit Milstein
 Division of Special Pathogen and Transplant Products
 Office of Antimicrobial Products
 Center for Drug Evaluation and Research

NDA 50-824
Compliance Pack for Omeprazole/clarithromycin/amoxicillin
DAVA Pharmaceuticals

RE: Request for revisions to the carton package, and submission of a physical sample of the complete carton blister card

Dear Dr. Hamet,

We refer to your NDA submission dated September 21, 2009, received September 22, 2009 for your omeprazole/clarithromycin/amoxicillin Compliance Pack.

In order to proceed with the timely review of your NDA, we request that you provide the following information by no later than June 7, 2010.

1. As previously communicated, we request you submit color mock-ups of the proposed container labels, as well as physical samples of the complete carton and one blister card so we can understand the shape of the carton.
2. We recommend that the established names of your product in the Principal Display Panel of the carton package be listed as follows:

Trademark[™]

Omeprazole delayed-release capsules, USP 20 mg

Clarithromycin tablets, USP 500 mg

Amoxicillin capsules, USP 500 mg

Please, let me know if you have any questions regarding this request.

Judit Milstein
Chief, Project Management Staff
Division of Special Pathogen and Transplant Products
301-796-0763

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	ORIG-1	DAVA PHARMACEUTICA LS INC	OMEPRAZOLE 25MG/AMOXOCILLIN 500MG/CLARITHROMYCIN 500MG

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/s/

JUDIT R MILSTEIN

06/03/2010

Request revisions to carton package and physical samples of the carton, blister pack.

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (<i>Office/Division</i>): OND/Maternal Health Staff		FROM (<i>Name, Office/Division, and Phone Number of Requestor</i>): Renata Albrecht, MD, Director, Division of Special Pathogen and Transplant Products		
DATE 4/23/10	IND NO.	NDA NO. 50-824	TYPE OF DOCUMENT Content of Labeling	DATE OF DOCUMENT
NAME OF DRUG Omeprazole/amoxicillin/ clarithromycin		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG Treatment of H. pylori	DESIRED COMPLETION DATE 5/24/10
NAME OF FIRM: DAVA Pharmaceuticals				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL	<input type="checkbox"/> PRE-NDA MEETING	<input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER		
<input type="checkbox"/> PROGRESS REPORT	<input type="checkbox"/> END-OF-PHASE 2a MEETING	<input type="checkbox"/> FINAL PRINTED LABELING		
<input type="checkbox"/> NEW CORRESPONDENCE	<input type="checkbox"/> END-OF-PHASE 2 MEETING	<input type="checkbox"/> LABELING REVISION		
<input type="checkbox"/> DRUG ADVERTISING	<input type="checkbox"/> RESUBMISSION	<input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE		
<input type="checkbox"/> ADVERSE REACTION REPORT	<input type="checkbox"/> SAFETY / EFFICACY	<input type="checkbox"/> FORMULATIVE REVIEW		
<input type="checkbox"/> MANUFACTURING CHANGE / ADDITION	<input type="checkbox"/> PAPER NDA	<input checked="" type="checkbox"/> OTHER (<i>SPECIFY BELOW</i>):		
<input type="checkbox"/> MEETING PLANNED BY	<input type="checkbox"/> CONTROL SUPPLEMENT			
II. BIOMETRICS				
<input type="checkbox"/> PRIORITY P NDA REVIEW	<input type="checkbox"/> CHEMISTRY REVIEW			
<input type="checkbox"/> END-OF-PHASE 2 MEETING	<input type="checkbox"/> PHARMACOLOGY			
<input type="checkbox"/> CONTROLLED STUDIES	<input type="checkbox"/> BIOPHARMACEUTICS			
<input type="checkbox"/> PROTOCOL REVIEW	<input type="checkbox"/> OTHER (SPECIFY BELOW):			
<input type="checkbox"/> OTHER (SPECIFY BELOW):				
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION	<input type="checkbox"/> DEFICIENCY LETTER RESPONSE			
<input type="checkbox"/> BIOAVAILABILITY STUDIES	<input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS			
<input type="checkbox"/> PHASE 4 STUDIES	<input type="checkbox"/> IN-VIVO WAIVER REQUEST			
IV. DRUG SAFETY				
<input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL	<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY			
<input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES	<input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE			
<input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (<i>List below</i>)	<input type="checkbox"/> POISON RISK ANALYSIS			
<input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP				
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL	<input type="checkbox"/> NONCLINICAL			
COMMENTS / SPECIAL INSTRUCTIONS:				
NDA 50-824, submitted on 9/21/09, received on 9/22/09, provides for the co-packaging of Omeprazole/amoxicillin/clarithromycin for the treatment of patients with H pylori infection and duodenal ulcer disease (active or one-year history of duodenal ulcer) to eradicate H pylori in adults.				
PDUFA Goal Date: July 22, 2010				
The Division requests your input on the appropriateness of the proposed language in the following sections of the content of labeling, and suggestions for alternative language when necessary.				
(b) (4)				
28 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page				

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	ORIG-1	DAVA PHARMACEUTICA LS INC	OMEPRAZOLE 25MG/AMOXOCILLIN 500MG/CLARITHROMYCIN 500MG

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/s/

JUDIT R MILSTEIN

04/23/2010

Consult to Maternal Health Team on content of labeling sections

REQUEST FOR DDMAC LABELING REVIEW CONSULTATION

****Please send immediately following the Filing/Planning meeting****

TO:

CDER-DDMAC-RPM

FROM: (Name/Title, Office/Division/Phone number of requestor)

Judit Milstein, Chief Project Management Staff

Division of Special Pathogen and Transplant Products (DSPTP)

REQUEST DATE
January 15, 2010

IND NO.

NDA/BLA NO.
50824

TYPE OF DOCUMENTS
(PLEASE CHECK OFF BELOW)

NAME OF DRUG

Omeprazole/Clarithromycin/
Amoxicillin-

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE
(Generally 1 week before the wrap-up meeting)

April 20, 2010

NAME OF FIRM:

DAVA Pharmaceuticals

PDUFA Date: July 22, 2010

Division Goal date-June 25, 2010

TYPE OF LABEL TO REVIEW

TYPE OF LABELING:

(Check all that apply)

PACKAGE INSERT (PI)

PATIENT PACKAGE INSERT (PPI)

CARTON/CONTAINER LABELING

MEDICATION GUIDE

INSTRUCTIONS FOR USE(IFU)

TYPE OF APPLICATION/SUBMISSION

ORIGINAL NDA/BLA

IND

EFFICACY SUPPLEMENT

SAFETY SUPPLEMENT

LABELING SUPPLEMENT

PLR CONVERSION

REASON FOR LABELING CONSULT

INITIAL PROPOSED LABELING

LABELING REVISION

EDR link to submission:

http://edr.fda.gov:7777/edr/EDR_Main.jsp

Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. The DDMAC reviewer will contact you at a later date to obtain the substantially complete labeling for review.

COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: [Insert Date]

Labeling Meetings: January 24, March 23, April 6, April 20, May 4, May 18, 2010

Wrap-Up Meeting: May 4, 2010

SIGNATURE OF REQUESTER

SIGNATURE OF RECEIVER

METHOD OF DELIVERY (Check one)

eMAIL

HAND

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	ORIG-1	DAVA PHARMACEUTICA LS INC	OMEPRAZOLE 25MG/AMOXOCILLIN 500MG/CLARITHROMYCIN 500MG

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/s/

JUDIT R MILSTEIN
01/15/2010
Consult to DDMAC-Labeling



NDA 50-824

FILING COMMUNICATION

DAVA Pharmaceuticals, Inc.
Attention: Susan Hamet
Vice President, Regulatory Affairs
Parker Plaza
400 Kelby Street, 10th Floor
Fort Lee, NJ 07024

Dear Ms. Hamet:

Please refer to your new drug application (NDA) dated September 21, 2009, received September 22, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for a Patient Compliance Pack containing omeprazole delayed-release tablets 20 mg, clarithromycin tablets 500 mg, and amoxicillin capsules, 500 mg.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is **Standard**. Therefore, the user fee goal date is July 22, 2010.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which include the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by June 11, 2010.

Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

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 indications in pediatric patients unless this requirement is waived, deferred, or inapplicable.



Once we have reviewed your revised request, we will notify you if [redacted] a pediatric drug development plan is required.

In addition, during our filing review we have identified the following potential review issues

1. Issues identified by the CMC Review team and conveyed to you in correspondence dated October 28, 2009 and November 16, 2009.

Provide a list of all manufacturing and testing sites for omeprazole, clarithromycin, and amoxicillin drug substance (and contract sites, if necessary, including those not previously submitted for drug product) for the proposed products in the Patient Compliance Pack. Please, also specify the responsibilities at each site, and include contact information (name, fax number) and a statement of inspection readiness.

We note that you responded to this request in your submission dated November 23, 2009.

2. Issues identified by the Clinical Review Team and conveyed to you in correspondence dated November 17, 2009.

Please address how each component of the co-packaged product contributes to the effect of the co-packaged product. This information can be provided from studies conducted or from published literature references.

We note that the due date for this request is January 3, 2010.

3. Labeling issues

- a. We note that your paper submission contains several different versions of the proposed Physician Labeling Rule (PLR) package insert and the version that was provided electronically does contain neither the **HIGHLIGHTS OF PRESCRIBING INFORMATION** nor the **FULL PRESCRIBING INFORMATION: CONTENTS** sections. Please, submit an electronic version of the PLR, in Word format, which

complies with the requirements of the Final Rule: Requirements on the Content and Format of Labeling for Human Prescription Drug and Biological Products, published January 24, 2006.

- b. This revised labeling should contain all labeling information from the three individual package inserts (omeprazole, amoxicillin, clarithromycin) pertinent to the proposed indication and should omit information not pertinent to the proposed indication.
- c. Provide copy of the most recent versions of the approved labels for each of the three drugs in the proposed compliance pack (i.e. omeprazole, clarithromycin, and amoxicillin.)

We request you provide this information by January 3, 2010.

If you have any questions, call Judit Milstein, Chief Project Management Staff, at (301) 796-0763.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, MD
Director
Division of Special Pathogen and Transplant
Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-50824

ORIG-1

DAVA
PHARMACEUTICA
LS INC

OMEPRAZOLE
25MG/AMOXOCILLIN
500MG/CLARITHROMYCIN
500MG

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/s/

RENATA ALBRECHT
12/04/2009



Food and Drug Administration
 Center for Drug Evaluation and Research
 Office of Antimicrobial Products

FACSIMILE TRANSMITTAL SHEET

DATE: November 17, 2009

To: Susan Hamet, Vice President Regulatory Affairs	From: Judit Milstein, Chief Project Management Staff
Company: DAVA Pharmaceuticals	Division of Special Pathogen and Transplant Products
Fax Number: 201-592-4640	Fax Number: 301-796-9881
Phone Number: 201-592-4476	Phone Number: 301-796-1600

Subject: Request for additional information

Total no. of pages including cover: 3

Document to be mailed: YES NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 301-796-1600. Thank you.

If you have any questions regarding the contents of this transmission, please contact me at 301-796-1600.

Judit Milstein
 Division of Special Pathogen and Transplant Products
 Office of Antimicrobial Products
 Center for Drug Evaluation and Research

NDA 50-824
Compliance Pack for Omeprazole/clarithromycin/amoxicillin
DAVA Pharmaceuticals

RE: Request for additional information

Dear Dr. Hamet,

We refer to your NDA submission dated September 21, 2009, received September 22, 2009 for your omeprazole/clarithromycin/amoxicillin Compliance Pack.

In order to proceed with the timely review of your NDA, we request that you provide the following information by no later than January 3, 2010.

Please address how each component of the co-packaged product contributes to the effect of the co-packaged product. We would expect that this be done by a comparison of the co-packaged products to each pair of drugs (i.e., co-packaged product vs. amoxicillin plus clarithromycin, co-packaged product vs. amoxicillin plus omeprazole, and co-packaged product vs. omeprazole plus clarithromycin). In each comparison the co-packaged product should be superior to the pair of drugs. This information can be supported by literature references.

Please, let me know if you have any questions regarding this request.

Judit Milstein
Chief, Project Management Staff
Division of Special Pathogen and Transplant Products
301-796-0763

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	ORIG-1	DAVA PHARMACEUTICA LS INC	OMEPRAZOLE 25MG/AMOXOCILLIN 500MG/CLARITHROMYCIN 500MG

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/s/

JUDIT R MILSTEIN
11/17/2009
Information Request



NDA 50-824

INFORMATION REQUEST

DAVA Pharmaceuticals, Inc.
Attention: Susan F. Hamet
Vice President, Regulatory Affairs
Parker Plaza
400 Kelby Street, 10th Floor
Fort Lee, New Jersey 07024

Dear Ms. Hamet:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for "TTBN", a Patient Compliance Pack consisting of Omeprazole Delayed-Release Capsules USP 20 mg, Clarithromycin Tablets USP, 500 mg, and Amoxicillin Capsules USP, 500 mg.

We also refer to the Information Request letter dated September 16, 2009, requesting that you provide in your NDA resubmission "all drug substance and drug manufacturing, testing, packaging and labeling sites relevant to the omeprazole, clarithromycin and amoxicillin drug products in the Patient Compliance Pack."

We note that you responded to the Agency's request in your resubmission dated September 21, 2009 (Exhibit 9). In this submission you stated that "sites for active drug substances and finished products may be considered as proprietary under each of the component finished product manufacturers' ANDAs," and instead you submitted Right of Reference to each finished product component ANDA. This information is not sufficient to support your NDA, as the names and addresses of all drug manufacturing and testing sites relevant to the omeprazole, clarithromycin and amoxicillin need to be included in NDA 50-824 in order to continue with the review of this application.

Based on this deficiency, Ms. Jeannie David contacted Ms. Stacy Bate, Regulatory Affairs Manager and requested you submit all drug substance manufacturing and testing sites relevant to the omeprazole, clarithromycin, and amoxicillin included in your proposed Patient Compliance Pack. She also requested that you include contact information (name, fax number) and a statement of inspection readiness.

During this telephone conversation, Ms. Bate offered to make follow up requests with the ANDA holders to obtain the drug substance manufacturing and testing sites (contract sites, if necessary, including those not previously submitted for drug product), and submit this information to the NDA as soon as possible.

In order to proceed with the timely review of NDA 50-824, we request that you provide the following information no later than November 11, 2009.

Provide a list of all manufacturing and testing sites for omeprazole, clarithromycin, and amoxicillin drug substance (and contract sites, if necessary, including those not previously submitted for drug product) for the proposed products in the Patient Compliance Pack. Please, also specify the responsibilities at each site, and include contact information (name, fax number) and a statement of inspection readiness.

If you have any questions regarding this letter, please call Jeannie David, Regulatory Project Manager, Office of New Drug Quality Assessment, at (301) 796-7472.

Sincerely,

{See appended electronic signature page}

Stephen Miller, Ph.D.
Acting Chief, Branch IV
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	ORIG-1	DAVA PHARMACEUTICA LS INC	AMOXICILLIN CAP 500MG/CLARITHROMYCIN TAB

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/s/

RAPTI D MADURawe
10/28/2009
for Steve Miller

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	ORIG-1	DAVA PHARMACEUTICA LS INC	AMOXICILLIN CAP 500MG/CLARITHROMYCIN TAB

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/s/

JUDIT R MILSTEIN

10/26/2009

Information request- [REDACTED] (b) (4)



NDA 50-824

NDA ACKNOWLEDGMENT

DAVA Pharmaceuticals, Inc.
Attention: Susan Hamet
Vice President, Regulatory Affairs
Parker Plaza
400 Kelby Street, 10th Floor
Fort Lee, NJ 07024

Dear MS. Hamet:

We have received your new drug application (NDA) pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Patient Compliance Pack (omeprazole delayed-release tablets, clarithromycin tablets and amoxicilling capsules, 20mg/500 mg/500mg.)

Date of Application: September 21, 2009

Date of Receipt: September 22, 2009

Our Reference Number: NDA 50-824

We note that this application originally submitted on June 18, 2009, received on June 19, 2009, was filed on August 18, 2009. We also acknowledge that due to requirements of the Medicare Modernization Act of 2003, you withdrew this application on August 20, 2009, and resubmitted the application with revised Listed Drug information.

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html>.

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Special Pathogen and Transplant Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/cder/ddms/binders.htm>.

If you have any questions, call me at (301) 796-0763.

Sincerely,

{See appended electronic signature page}

Judit Milstein
Chief, Project Management Staff
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	ORIG-1	DAVA PHARMACEUTICA LS INC	AMOXICILLIN CAP 500MG/CLARITHROMYCIN TAB

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/s/

JUDIT R MILSTEIN

10/07/2009

Acknowledgment of resubmission of NDA



NDA 50-824

**ACKNOWLEDGE REQUEST
TO WITHDRAW PENDING NDA**

DAVA Pharmaceuticals, Inc.
Attention: Susan F. Hamet
Vice President, Regulatory Affairs
Parker Plaza
400 Kelby Street, 10th Floor
Fort Lee, New Jersey 07024

Dear Ms. Hamet:

We have received your August 20, 2009 correspondence on August 21, 2009 notifying us that you are withdrawing your new drug application (NDA) for a patient compliance pack consisting of Omeprazole Delayed-Release Capsules 20 mg, Clarithromycin Tablets, 500 mg, and Amoxicillin Capsules 500 mg. This application was filed on August 18, 2009.

In accordance with 21 CFR 314.65, this application is withdrawn as of August 21, 2009. 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 include

1. A list of all the reference listed drugs (RLDs) in FDA Form 356h
2. A list of all patent certifications for the RLDs listed in the FDA Form 356h
3. A revised User Fee Cover Sheet (FDA Form 3397)
4. FDA form 3674 titled "Requirements of ClinicalTrials.gov Data Bank"

If you have any questions, please call Christina H. Chi, Ph.D., Regulatory Health Project Manager, at (301) 796-1695.

Sincerely,

{See appended electronic signature page}

Judit Milstein
Chief, Project Management Staff
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	GI-1	DAVA PHARMACEUTICA LS INC	AMOXICILLIN CAP 500MG/CLARITHROMYCIN TAB

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/s/

JUDIT R MILSTEIN

09/23/2009

Acknowledgment of Withdrawal of a Pending Application



NDA 50-824

INFORMATION REQUEST

DAVA Pharmaceuticals, Inc.
Attention: Susan F. Hamet
Vice President, Regulatory Affairs
Parker Plaza
400 Kelby Street, 10th Floor
Fort Lee, New Jersey 07024

Dear Ms. Hamut:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for "TTBN", a Patient Compliance Pack consisting of Omeprazole Delayed-Release Capsules USP 20 mg, Clarithromycin Tablets USP, 500 mg, and Amoxicillin Capsules USP, 500 mg.

We also refer to the Establishment Listing provided in Attachment 1 to Form FDA 356h and have the following request for information.

- Please provide in your NDA resubmission the current establishment information for all drug substance and drug product manufacturing, testing, packaging and labeling sites relevant to the omeprazole, clarithromycin, and amoxicillin drug products proposed in the Patient Compliance Pack. For each establishment, provide a contact name and fax number relevant to that site, and state if that site is ready for inspection.

If you have any questions regarding this letter, please call Jeannie David, Regulatory Project Manager, Office of New Drug Quality Assessment, at (301) 796-7472.

Sincerely,

{See appended electronic signature page}

Stephen Miller, Ph.D.
Acting Chief, Branch IV
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	ORIG-1	DAVA PHARMACEUTICA LS INC	AMOXICILLIN CAP 500MG/CLARITHROMYCIN TAB

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/s/

STEPHEN P MILLER
09/16/2009
Concur



NDA 50-824

MEETING MINUTES

DAVA Pharmaceuticals, Inc.
Attention: Susan F. Hamet
Vice President, Regulatory Affairs
Parker Plaza
400 Kelby Street, 10th Floor
Fort Lee, New Jersey 07024

Dear Ms. Hamet:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for "TTBN", a co-packaged product consisting of Omeprazole Delayed-Release Capsules USP 20 mg, Clarithromycin Tablets USP, 500 mg, and Amoxicillin Capsules USP, 500 mg.

We also refer to the teleconference between representatives of your firm and the FDA on August 14, 2009. The purpose of the teleconference was to discuss deficiencies identified in NDA 50-824.

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

If you have any questions, please call Christina H. Chi, Ph.D., Regulatory Health Project Manager, at (301) 796-1695.

Sincerely,

{See appended electronic signature page}

Judit Milstein
Chief, Project Management Staff
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Minutes of the meeting

MEMORANDUM OF TELECONFERENCE MINUTES

TELECONFERENCE DATE: August 14, 2009

TIME: 12:00 - 1:00 PM

APPLICATION: NDA 50-824

PRODUCT NAME: “TTBN”, a co-packaged product consisting of Omeprazole Delayed-Release Capsules USP 20 mg, Clarithromycin Tablets USP, 500 mg, and Amoxicillin Capsules USP, 500 mg.

TELECONFERENCE CHAIR: Janice Weiner, JD, MPH

TELECONFERENCE RECORDER: Christina H. Chi, Ph.D.

FDA ATTENDEES:

Janice Weiner, J.D., M.P.H.	Regulatory Counsel, ORP/DRP I
Michael D. Jones	Special Assistant, ORP
Kim M. Quaintance	Associate Director for Regulatory Affairs, OND
Beth A. Duvall Miller	Team Leader, Regulatory Affairs Team, OND
David L. Roeder	Consumer Safety Officer, OND/OAP
Joette M. Meyer	Team Leader, OND/OAP/DSPTP
Tafadzwa Vargas-Kasambira, M.D.	Medical Officer, OND/OAP/DSPTP
Judit Milstein	Chief, Project Management Staff, OND/OAP/DSPTP
Christina H. Chi, Ph.D.	Regulatory Health Project Manager, OND/OAP/DSPTP

EXTERNAL CONSTITUENT ATTENDEES:

A. DAVA Pharmaceuticals, Inc.:

Susan F. Hamet	Vice President, Regulatory Affairs
Stacy Bate	Manager, Regulatory Affairs

B. DAVA Pharmaceuticals, Inc. Regulatory Counsel:

Nathan Beaver, J.D.	Partner, Foley & Lardner, LLP
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BACKGROUND:

On June 18, 2009, DAVA Pharmaceuticals (DAVA) submitted NDA 50-824 for “TTBN”, a proposed co-packaged product consisting of 3 approved ANDA products: Omeprazole Delayed-Release Capsules USP 20 mg, Clarithromycin Tablets USP, 500 mg, and Amoxicillin Capsules USP, 500 mg. This cover letter accompanying this 505(b)(2) application stated:

“...the basis for submission for this 505(b)(2) NDA is the FDA-approved labeling for Omeprazole Delayed-Release Capsules USP, 20 mg, which specifies the use of triple-therapy (omeprazole, clarithromycin and amoxicillin) for the treatment of patients with H. pylori infection and duodenal ulcer disease (active or up to 1-year history) to eradicate H. pylori in adults. DAVA’s proposed Physician’s Insert (Content of Labeling) was prepared based upon the currently approved labeling for each of the three (3) ANDA-approved finished drug products which are the component products of DAVA’s Patient Compliance Pack, as well as recommendations provided by the Agency.”

Form 356h identified only “Prilosec[®] Content of Labeling” held by AstraZeneca as the listed drug relied upon for this 505(b)(2) application. Further, DAVA submitted a “paragraph I” patent certification (such patent information has not been filed) which would be unacceptable if DAVA intended to rely upon the Agency’s finding of safety and effectiveness for Prilosec (NDA 19-810) to support approval of its proposed 505(b)(2) application given that multiple patents are listed in FDA’s Approved Drug Products with Therapeutic Equivalence Evaluations (the Orange Book) for NDA 19-810.

This teleconference was requested by the Agency to discuss certain deficiencies identified in the NDA submission.

MEETING OBJECTIVES:

To discuss with the applicant the deficiencies identified in NDA 50-824.

DISCUSSION POINTS:

The Agency explained the following points to DAVA and their regulatory counsel:

1. DAVA’s NDA 50-824 was submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), and this proposed co-packaged product is composed of 3 drug products that have been approved in ANDAs. Based on this submission, it appears that DAVA intends to rely upon the Agency’s finding of safety and effectiveness for each of the reference listed drugs (RLDs) that were the basis for submission of each of the ANDA products in the proposed co-packaged product. However, DAVA’s submission does not identify these RLDs as the listed drugs relied upon for its 505(b)(2) application.

2. A 505(b)(2) application contains “full reports of investigations” of safety and effectiveness, where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use. Accordingly, reliance only on the approved ANDAs is not acceptable to support your proposed 505(b)(2) application. DAVA would need to identify the NDA product that was the basis for submission (the RLD) for each of the ANDA products in the proposed co-packaged product as the listed drugs relied upon to support its proposed 505(b)(2) application.
3. DAVA identified “Prilosec® Content of Labeling” on Form 356h as the listed drug relied upon for this 505(b)(2) application. Although DAVA indicated during the teleconference that they believed they had identified Prilosec as a listed drug relied upon for this 505(b)(2) application, FDA noted that this was unclear (especially in light of the paragraph I certification which is inconsistent with the multiple unexpired patents listed in the Orange Book for NDA 19-810 for Prilosec). FDA advised that DAVA had not identified a listed drug relied upon for the clarithromycin and amoxicillin components of this proposed co-packaged product.
4. If DAVA intends to seek approval for a co-packaged product composed of Omeprazole Delayed-Release Capsules 20 mg, Clarithromycin Tablets, 500 mg, and Amoxicillin Capsules, 500 mg, in reliance on the Agency’s finding of safety and effectiveness for the NDA products upon which the ANDA approvals were based, DAVA would need to identify each of the RLDs for the ANDAs as listed drugs relied upon and provide an appropriate patent certification or statement for each patent listed in the Orange Book for each listed drug relied upon. However, we interpret section 505(b)(4)(A) of the FDCA, added by the Medicare Modernization Act (MMA), to preclude a 505(b)(2) applicant from amending or supplementing a 505(b)(2) application to seek approval of a drug that relies on the Agency’s finding of safety and effectiveness for a drug that is different from the drug identified in a previous submission of the application. Accordingly, the identification of additional listed drugs relied upon is not the type of change that may be made in an amendment to a 505(b)(2) application. DAVA may elect to withdraw and resubmit its 505(b)(2) application to identify each of the RLDs for the ANDA products as listed drugs relied upon in support of its 505(b)(2) application.

DAVA noted that they believed they had adequately identified Prilosec as a listed drug relied upon, and inquired whether an amendment to identify two additional listed drugs relied upon would be precluded by section 505(b)(4)(A) of the FDCA. FDA noted that it does not currently interpret section 505(b)(4)(A) to permit such an amendment, and referred DAVA to the citizen petition response regarding venlafaxine (Docket No. FDA-2008-P-0329), specifically footnote 30 on page 16.

5. With respect to Prilosec, which was not clearly identified as a listed drug relied upon, we noted that a paragraph I certification would not be an acceptable patent certification because there are several unexpired patents listed in the Orange Book for NDA 19-810. Thus, DAVA would have the option of submitting a paragraph III certification, paragraph

IV certification, or, if method-of-use patents were identified in the Orange Book, a 505(b)(2)(B) statement.

6. In the cover letter of the submission, DAVA indicated that this 505(b)(2) application represented the first in DAVA's initiative to seek approval for co-packaged products composed of drugs approved in ANDAs. FDA advised that the regulatory comments provided during this teleconference (including but not limited to identification of the listed drugs relied upon) should inform any other future 505(b)(2) submissions for co-packaged products composed of drug products approved in ANDAs.
7. If the application is withdrawn before the filing date of August 18, 2009, DAVA will receive a refund of 75% of the fee. If DAVA elects to resubmit the application, upon resubmission, a full (100%) user fee will have to be paid.

If the application is withdrawn after the filing date, DAVA will receive no refund. Further, in this situation, if the application is amended and resubmitted later on, only with an amendment of the required RLD and patent information (e.g., the application is for the same product, the same dosage, the same route of administration, and the same indication), the user fee is considered paid according to section 736(a)(1)(C) of the FDCA, and no additional fee will be required.

8. The user fee clock will start anew if the application is resubmitted after it is withdrawn. This is the case whether the application is withdrawn before or after filing.
9. If DAVA elects to resubmit its 505(b)(2) application, please include the following information in the resubmission:
 - Identify all listed drugs relied upon in FDA form 356h
 - Provide appropriate patent certifications or statements for each of the listed drugs relied upon
 - A reference to the withdrawal of the application in the cover letter
 - A new user fee cover sheet (FDA form 3397)
 - A list of the Clinical trials (FDA form 3674)

Post-Meeting Note:

The Division recommends that sponsors considering the submission of an application through the 505(b)(2) pathway consult the Agency's regulations at 21 CFR 314.54, and the October 1999 Draft Guidance for Industry "Applications Covered by Section 505(b)(2)" available at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50824	ORIG-1	DAVA PHARMACEUTICA LS INC	AMOXICILLIN CAP 500MG/CLARITHROMYCIN TAB

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/s/

JUDIT R MILSTEIN
09/15/2009
Minutes of teleconference



NDA 50-824

NDA ACKNOWLEDGMENT

DAVA Pharmaceuticals, Inc.
Attention: Susan F. Hamet
Vice President, Regulatory Affairs
Parker Plaza
400 Kelby Street, 10th Floor
Fort Lee, New Jersey 07024

Dear Ms. Hamet:

We have received your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Patient Compliance Pack (Omeprazole Delayed-Release Capsules USP 20 mg, Clarithromycin Tablets USP, 500 mg, and Amoxicillin Capsules USP, 500 mg).

Date of Application: June 18, 2009

Date of Receipt: June 19, 2009

Our Reference Number: NDA 50-824

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on August 18, 2009 in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

Please note that the pre-assigned NDA number (b) (4) is no longer valid and the new number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Special Pathogen and Transplant Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/cder/ddms/binders.htm>.

If you have any questions, please call Christina H. Chi, Ph.D., Regulatory Health Project Manager, at (301) 796-1695.

Sincerely,

{See appended electronic signature page}

Judit Milstein
Chief, Project Management Staff
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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

/s/

Judith Milstein
7/23/2009 01:19:33 PM
NDA 50-824 NDA Acknowledgment Letter