

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

204150Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 204150

SUPPL #

HFD # 130

Trade Name

Generic Name Desvenlafaxine Extended-Release 50mg and 100mg Tablets

Applicant Name Alembic Pharmaceuticals Limited

Approval Date, If Known 03/04/13

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.

The sponsor solely used PRISTIQ as a RLD and submitted bioequivalence data comparing their product to the innovator's product to support approval.

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?

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# 021922

PRISTIQ (desvenlafaxine succinate extended-release tablets)

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#

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: Kofi B. Ansah, Pharm.D., CDR USPHS
Title: Senior Regulatory Project Manager
Date: 03/04/13

Name of Office/Division Director signing form: Mitchell V. Mathis, M.D., CAPT USPHS
Title: Director (acting), Division of Psychiatry Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

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

/s/

KOFI B ANSAH
03/04/2013

MITCHELL V Mathis
03/04/2013

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 204150 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type:
Proprietary Name: Established/Proper Name: Desvenlafaxine Extended-Release Dosage Form: Tablets		Applicant: Alembic Pharmaceuticals Limited Agent for Applicant (if applicable): Hari Nagaradona, Ph.D. , Director, Regulatory Affairs; INC Research, LLC , 7361 Calhoun Place, Suite 500, Rockville, MD 20855
RPM: Kofi Ansah, Pharm.D.		Division: Division of Psychiatry Products
<p><u>NDA and NDA Efficacy Supplements:</u></p> <p>NDA Application Type: <input 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)</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><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></p> <p>Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s):</p> <p>NDA 21992 – PRISTIQ (desvenlafaxine) Extended-Release Tablets</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>This current product is the “Desvenlafaxine (base) Extended-Release Tablets</p> <p><input type="checkbox"/> This application does not reply upon a listed drug. <input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input checked="" type="checkbox"/> This application relies on (explain) The Agency’s findings of Safety and Efficacy from the review if the RLD (i.e., PRISTIQ).</p> <p><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft² 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 type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check:</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>March 4, 2013</u> 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR

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.

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).

<ul style="list-style-type: none"> Previous actions (<i>specify type and date for each action taken</i>) 	<input type="checkbox"/> None TA - 12/21/12
<ul style="list-style-type: none"> 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 _____ 	<input type="checkbox"/> Received
<ul style="list-style-type: none"> Application Characteristics³ 	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</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> <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> 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> REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Communication Plan <input type="checkbox"/> ETASU <input checked="" type="checkbox"/> MedGuide w/o REMS <input type="checkbox"/> REMS not required </p> <p>Comments:</p>	
<ul style="list-style-type: 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) 	<input type="checkbox"/> Yes, dates
<ul style="list-style-type: none"> BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>) 	<input type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> Public communications (<i>approvals only</i>) 	
<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

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.

❖ 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 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"/> Not applicable because drug is an old antibiotic.
<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 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 ⁴	03/04/13 (date signed)
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 Letter – 03/04/13 & TA Letter - 12/21/12
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. 	2/28/13 agreed upon labeling (with minor revisions on 3/4/13 - see AP Letter)
<ul style="list-style-type: none"> Original applicant-proposed labeling 	2/27/13 revised resubmission label 12/20/12 revised original label-TA 02/29/12 original submission label
<ul style="list-style-type: none"> Example of class labeling, if applicable 	PRISTIQ Labeling (S-034)

⁴ Fill in blanks with dates of reviews, letters, etc.

<ul style="list-style-type: none"> ❖ 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>) 	<input checked="" type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input 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. 	see above
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	see above
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	see above
<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 	02/28/13; 11/29/12
<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>) • Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name. 	N/A
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input checked="" type="checkbox"/> RPM 07/17/12 <input checked="" type="checkbox"/> DMEPA 11/04/12 & 12/13/12 <input checked="" type="checkbox"/> DMPP/PLT (DRISK) 11/30/12 <input checked="" type="checkbox"/> ODPD (DDMAC) 12/03/12 (PI & Carton/Container Labels) <input checked="" type="checkbox"/> SEALD 02/28/13 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
<ul style="list-style-type: none"> ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁵/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) 	05/11/12
<ul style="list-style-type: none"> ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>) 	<input type="checkbox"/> Not a (b)(2) AP - 02/20/13 TA - 12/05/12 <input type="checkbox"/> Not a (b)(2) 03/01/13
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) 	<input checked="" type="checkbox"/> Included 03/04/13
<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 checked="" 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 11/14/12 (<u>Peds Page/Record in DARRTS as peds entry</u>) If PeRC review not necessary, explain: _____ • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input checked="" type="checkbox"/> Included

⁵ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ 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
❖ Outgoing communications <i>(letters, including response to FDRR (do not include previous action letters in this tab), emails, faxes, telecons)</i>	Included (see action package)
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• Regulatory Briefing <i>(indicate date of mtg)</i>	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> N/A or no mtg 02/21/13
• Pre-NDA/BLA meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> No mtg
• EOP2 meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) <i>(indicate dates of mtgs)</i>	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 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 N/A
Division Director Summary Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 03/04/13
Cross-Discipline Team Leader Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 12/20/12
PMR/PMC Development Templates <i>(indicate total number)</i>	<input type="checkbox"/> None
Clinical Information⁶	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) <i>(indicate date for each review)</i>	CDTL Review – 12/20/12
• Clinical review(s) <i>(indicate date for each review)</i>	11/28/12
• 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 type="checkbox"/> and include a review/memo explaining why not <i>(indicate date of review/memo)</i>	11/28/12 – See Clinical Review
❖ 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 type="checkbox"/> Not applicable <input checked="" type="checkbox"/> None
❖ Risk Management	
• 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

⁶ Filing reviews should be filed with the discipline reviews.

❖ OSI Clinical Inspection Review Summary(ies) (include copies of OSI letters to investigators)	<input checked="" type="checkbox"/> None requested
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None 11/29/12 (Primary Review); (Filing Review)
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of OSI letters)	<input type="checkbox"/> None 10/09/12 & 04/11/12
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Supervisory Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None 12/10/12 (Memo to File); 05/14/12 (Filing Review)
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary (include copies of OSI letters)	<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>	<input type="checkbox"/> None CMC- 11/26/12 (Primary Review); 03/08/12 (Filing Review) Biopharmaceutics - 11/25/12 (Primary Review); 04/24/12 (filing Review)
❖ 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 (OMPQ/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 type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>	11/26/12 & 03/08/12 (see CMC Review)
<input type="checkbox"/> Review & FONSI <i>(indicate date of review)</i>	
<input type="checkbox"/> Review & Environmental Impact Statement <i>(indicate date of each review)</i>	
❖ Facilities Review/Inspection	
<input type="checkbox"/> NDAs: Facilities inspections (include EER printout) <i>(date completed must be within 2 years of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁷)</i>	Date completed: 09/24/12 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER <i>(date of most recent TB-EER must be within 30 days of action date) (original and supplemental BLAs)</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 type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

⁷ 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.

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy 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).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

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

/s/

KOFI B ANSAH
03/04/2013

From: [Nagaradona, Hari](#)
To: [David, Paul A](#); [Ansah, Kofi](#)
Subject: RE: Proposed Labeling (PI; MG; & Bottle/Container Labels) for Agreement -- NDA 204150/ALEMBIC/Desvenlafaxine Extended-Release/
Date: Monday, March 04, 2013 1:20:15 PM

Dear Paul

We agree with your assessment and do not have any concerns.

Thanks and Best regards,

Hari

From: David, Paul A [<mailto:Paul.David@fda.hhs.gov>]
Sent: Monday, March 04, 2013 1:07 PM
To: Nagaradona, Hari; Ansah, Kofi
Subject: RE: Proposed Labeling (PI; MG; & Bottle/Container Labels) for Agreement -- NDA 204150/ALEMBIC/Desvenlafaxine Extended-Release/

Hari,
I did find one mistake in the labeling we provided to you. It should be 7 days (b) (4)
 on page 16 (see attached) of the label. This would be consistent with the HL.

Let me know if you have any concerns with this revision.

Thanks,
Paul

From: Nagaradona, Hari [<mailto:Hari.Nagaradona@INCRResearch.com>]
Sent: Monday, March 04, 2013 12:34 PM
To: Ansah, Kofi
Cc: David, Paul A
Subject: RE: Proposed Labeling (PI; MG; & Bottle/Container Labels) for Agreement -- NDA 204150/ALEMBIC/Desvenlafaxine Extended-Release/

Dear Kofi

The applicant Alembic is in agreement with changes.

Thanks and Best regards,

Hari

From: Ansah, Kofi [<mailto:Kofi.Ansah@fda.hhs.gov>]
Sent: Monday, March 04, 2013 11:37 AM
To: Nagaradona, Hari
Cc: David, Paul A
Subject: RE: Proposed Labeling (PI; MG; & Bottle/Container Labels) for Agreement -- NDA 204150/ALEMBIC/Desvenlafaxine Extended-Release/

Importance: High

Hi Hari,

I was writing to you as your email came through so I had to stop and respond to that instead. Things are moving along and we are on track to issuing our Action letter sometime today. But please not the following:

We have made the following minor revision to the PI with regards to 7.1; everything else is as agreed on 2/28/13. Please confirm agreement to this change so that we can finalize things on our side. A word copy of the PI with this change tracked is attached for your convenience and I have also attached the MG and Labels so you have everything in one place.

7.1 Monoamine Oxidase Inhibitors (MAOI)

Do not use MAOIs intended to treat psychiatric disorders with desvenlafaxine or within (b) (4) days of stopping treatment with desvenlafaxine. Do not use desvenlafaxine within 14 days of stopping an MAOI intended to treat psychiatric disorders. In addition, do not start desvenlafaxine in a patient who is being treated with linezolid or intravenous methylene blue (b) (4)

[see Dosage and Administration (2.6), Contraindications (4) and Warnings and Precautions (5.2)]

Please affirm agreement as soon as soon as possible.

Thanks,
Kofi.

From: Nagaradona, Hari [<mailto:Hari.Nagaradona@INCRsearch.com>]
Sent: Monday, March 04, 2013 11:07 AM
To: Ansah, Kofi
Cc: David, Paul A
Subject: RE: Proposed Labeling (PI; MG; & Bottle/Container Labels) for Agreement -- NDA 204150/ALEMBIC/Desvenlafaxine Extended-Release/

Dear Kofi

How is the final approval action letter coming along? We hope to receive today and let us know if you have any questions.

Thanks and Best regards,

Hari

From: Ansah, Kofi [<mailto:Kofi.Ansah@fda.hhs.gov>]
Sent: Friday, March 01, 2013 8:06 AM
To: Nagaradona, Hari
Cc: David, Paul A
Subject: Re: Proposed Labeling (PI; MG; & Bottle/Container Labels) for Agreement -- NDA 204150/ALEMBIC/Desvenlafaxine Extended-Release/

Hari,

Please be sure to wait for our Action Letter with labeling as there could still be some last minute minor changes/edits.

Thanks,
Kofi.

From: Nagaradona, Hari [<mailto:Hari.Nagaradona@INCResearch.com>]
Sent: Friday, March 01, 2013 07:30 AM
To: Ansah, Kofi
Cc: David, Paul A
Subject: RE: Proposed Labeling (PI; MG; & Bottle/Container Labels) for Agreement -- NDA 204150/ALEMBIC/Desvenlafaxine Extended-Release/

Dear Kofi

Please find below Alembic comments.

Alembic is in agreement on the text of attached proposed labeling and same shall be used for the commercial supplies. However, there would be Annual Reportable Changes in the final printed labeling (PI, MG and Bottle/ Container labels) Example:

 (b) (4)

Also, please let us know if above mail is sufficient or we have to submit the amendment in eCTD format.

Thanks and Best regards,

Hari

Hari Nagaradona, PhD | Director, Regulatory Affairs | Regulatory Strategy, Consulting and Submissions
INC Research, LLC
7361 Calhoun Place, Suite 500, Rockville, MD 20855 | USA
Tel: +1-301-296-1370 | Mobile:  (b) (6) | Fax: +1-301-838-3182
hari.nagaradona@incresearch.com | www.incresearch.com | **INC Research**®

From: Ansah, Kofi [<mailto:Kofi.Ansah@fda.hhs.gov>]
Sent: Thursday, February 28, 2013 9:29 PM
To: Nagaradona, Hari
Cc: David, Paul A
Subject: Proposed Labeling (PI; MG; & Bottle/Container Labels) for Agreement -- NDA 204150/ALEMBIC/Desvenlafaxine Extended-Release/

Hi Hari,

Attached is the proposed Labeling [i.e., current/revised USPI (or PI & MG), and Bottle/Container Labels (from 11-29-13)] for your application. Please confirm that we have agreement on this labeling sometime tomorrow.

Thanks,
Kofi.

Kofi Boadu Ansah, R.Ph., Pharm.D.

CDR, US Public Health Service

Regulatory Project Manager, Division of Psychiatry Products

FDA/Center for Drug Evaluation and Research, Office of Drug Evaluation-I

10903 New Hampshire Avenue, White Oak Bldg 22, Room 4109

Silver Spring, MD 20993 - 0002

Phone: (301) 796-4158

Fax: (301) 796-9838

Email: Kofi.Ansah@fda.hhs.gov

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/s/

KOFI B ANSAH
03/04/2013

From: Ansah, Kofi
To: "[Nagaradona, Hari](#)"
Cc: [David, Paul A](#)
Subject: Proposed Labeling (PI) for Formatting Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC
Date: Wednesday, February 27, 2013 5:03:00 PM
Attachments: [02-27-13_DPP_edits_02-21-13_Sponsor Revised_final-labeling-text-word-file.doc](#)

Hi Hari,

As per my earlier email, please find attached the proposed PI which includes our minor modifications. We need you to fix some formatting errors and return to us ASAP by early tomorrow for further review.

Please see imbedded comments for the formatting corrections in the attached PI but basically, we need you to fix the following:

1. Ensure removal of box/lines around TOC.
2. Move TOC to second page; ensuring that the HL columns remain even (or as close to even as possible).
3. Maintain the line(s) separating the TOC from the HL and FPI.

Please try your best to return this to us tomorrow as we need to route it to a different group for their review tomorrow. Let me know if you have any questions or issues with this request.

Thanks,
Kofi.

From: Ansah, Kofi
Sent: Wednesday, February 27, 2013 10:51 AM
To: 'Nagaradona, Hari'
Cc: David, Paul A
Subject: RE: Proposed Labeling (PI &MG) for Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC

Hi Hari,

I was just getting ready to send you an email. The revised USPI is still under review -- I may be sending it back to you with a very quick turn around for some formatting corrections.

Also, as per our acknowledgement Letter for your resubmission, the action date for this NDA is 3/4/13 and we are on track to taking action on that day, at this point. I will let you know if anything comes up or changes.

Thanks,
Kofi.

From: Nagaradona, Hari [<mailto:Hari.Nagaradona@INCRResearch.com>]
Sent: Wednesday, February 27, 2013 10:21 AM
To: Ansah, Kofi
Cc: David, Paul A
Subject: RE: Proposed Labeling (PI &MG) for Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC

Dear Kofi

Any update on the review of the labeling update? Are we on track to get approval by Mar 1 as the exclusivity is expected to expire?

Thanks and Best regards,

Hari

From: Ansah, Kofi [mailto:Kofi.Ansah@fda.hhs.gov]
Sent: Friday, February 22, 2013 8:55 AM
To: Nagaradona, Hari
Cc: David, Paul A
Subject: RE: Proposed Labeling (PI &MG) for Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC

Hi Hari,

Thank you for the prompt response. I will let you know if we have any questions or further information request. Take care and have a nice weekend.

Best Regards,
Kofi.

From: Nagaradona, Hari [mailto:Hari.Nagaradona@INCRResearch.com]
Sent: Friday, February 22, 2013 7:48 AM
To: Ansah, Kofi
Cc: David, Paul A
Subject: RE: Proposed Labeling (PI &MG) for Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC

Dear Kofi

Here the PI and the guide in track change as requested. We are submitting the labeling changes through gateway as well.

Thanks and Best regards,

Hari

Hari Nagaradona, PhD | Director, Regulatory Affairs | Regulatory Strategy, Consulting and Submissions
INC Research, LLC
7361 Calhoun Place, Suite 500, Rockville, MD 20855 | USA
Tel: +1-301-296-1370 | Mobile: (b) (6) | Fax: +1-301-838-3182
hari.nagaradona@incresearch.com | www.incresearch.com | **INC Research®**

From: Ansah, Kofi [mailto:Kofi.Ansah@fda.hhs.gov]
Sent: Thursday, February 21, 2013 1:14 PM
To: Nagaradona, Hari
Cc: David, Paul A

Subject: Re: Proposed Labeling (PI &MG) for Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC

Hari:

Yes, please do -- Thanks.

Kofi.

From: Nagaradona, Hari [<mailto:Hari.Nagaradona@INCRResearch.com>]
Sent: Thursday, February 21, 2013 01:02 PM
To: Ansah, Kofi
Cc: David, Paul A
Subject: RE: Proposed Labeling (PI &MG) for Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC

Thanks Kofi.

One more question. Should we submit the track change version as part of the submission too?

Thanks and Best regards,

Hari

From: Ansah, Kofi [<mailto:Kofi.Ansah@fda.hhs.gov>]
Sent: Thursday, February 21, 2013 12:58 PM
To: Nagaradona, Hari
Cc: David, Paul A
Subject: RE: Proposed Labeling (PI &MG) for Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC

Hari,

Noted -- Thank you. They should have known to do that though, you always want to include a tracked-changes version when it comes to labeling changes. Take care and talk to you later. They may go ahead and formally submit these revised proposed USPI to their NDA through the gateway.

Kofi.

From: Nagaradona, Hari [<mailto:Hari.Nagaradona@INCRResearch.com>]
Sent: Thursday, February 21, 2013 12:53 PM
To: Ansah, Kofi
Subject: RE: Proposed Labeling (PI &MG) for Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC

Kofi

I will contact the applicant and request the same. It may come to you tomorrow morning.

Thanks and Best regards,

Hari

From: Ansah, Kofi [<mailto:Kofi.Ansah@fda.hhs.gov>]
Sent: Thursday, February 21, 2013 12:37 PM
To: Nagaradona, Hari
Subject: RE: Proposed Labeling (PI &MG) for Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC

Hi Hari,

Thank you for the prompt turn-around ... I will get back to you on the question you posed below but in the meantime, could you provide a tracked-changes version of the word documents you sent ?

Thanks,
Kofi.

Kofi Boadu Ansah, R.Ph., Pharm.D.

CDR, US Public Health Service

Regulatory Project Manager, Division of Psychiatry Products

FDA/Center for Drug Evaluation and Research, Office of Drug Evaluation-I
10903 New Hampshire Avenue, White Oak Bldg 22, Room 4109

Silver Spring, MD 20993 - 0002

Phone: (301) 796-4158

Fax: (301) 796-9838

Email: Kofi.Ansah@fda.hhs.gov

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From: Nagaradona, Hari [<mailto:Hari.Nagaradona@INCRResearch.com>]
Sent: Thursday, February 21, 2013 8:59 AM
To: Ansah, Kofi
Subject: RE: Proposed Labeling (PI &MG) for Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC

Dear Kofi

The applicant has revised the labeling per your request. Find enclosed the revised files.

Do you want us to submit the same through gateway or should wait to receive your feedback first. Please clarify and confirm.

Thanks and Best regards,

Hari

Hari Nagaradona, PhD | Director, Regulatory Affairs | Regulatory Strategy, Consulting and Submissions

INC Research, LLC

7361 Calhoun Place, Suite 500, Rockville, MD 20855 | USA

Tel: +1-301-296-1370 | Mobile: (b) (6) Fax: +1-301-838-3182

hari.nagaradona@incresearch.com | www.incresearch.com | **INC Research®**

From: Ansah, Kofi [<mailto:Kofi.Ansah@fda.hhs.gov>]

Sent: Tuesday, February 19, 2013 12:24 PM

To: Nagaradona, Hari

Subject: Proposed Labeling (PI &MG) for Revisions -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC

Dear Hari:

As per our telephone conversation earlier today, please find attached the recently approved Pristiq Labeling (PI & MG) that we would like you to adapt yours to. Working off the Labeling that was attached to your TA Letter (dated 12/21/12; a copy of which is also attached for your convenience), please incorporate the language from the innovator's 2-14-13 labeling as applicable, except for the (b) (4) which we have already taken out of the attached Pristiq USPI.

We need a very quick turn-around on this so that we can move the process forward. I, therefore, ask that you make the requested changes and send us your revised draft back as soon as possible preferable by noon this Thursday, if at all possible. Let us know if this timeline does not work for you.

Thanks,
Kofi.

Kofi Boadu Ansah, R.Ph., Pharm.D.

CDR, US Public Health Service

Regulatory Project Manager, Division of Psychiatry Products

FDA/Center for Drug Evaluation and Research, Office of Drug Evaluation-I
10903 New Hampshire Avenue, White Oak Bldg 22, Room 4109

Silver Spring, MD 20993 - 0002

Phone: (301) 796-4158

Fax: (301) 796-9838

Email: Kofi.Ansah@fda.hhs.gov

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

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/s/

KOFI B ANSAH
03/01/2013



NDA 204150

**ACKNOWLEDGE --
CLASS 1 COMPLETE RESPONSE**

Alembic Pharmaceuticals Limited
Attention: Hari Nagaradona, Ph.D.
Director, Regulatory Affairs
INC Research, LLC
7361 Calhoun Place, Suite 500
Rockville, MD 20855

Dear Dr. Nagaradona:

We acknowledge receipt on January 4, 2013, of your January 4, 2013, resubmission to your new drug application submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Desvenlafaxine Extended-Release Tablets 50 mg and 100 mg.

We consider this a complete, class 1 response to our December 21, 2012, action letter. Therefore, the user fee goal date is March 4, 2013.

If you have any questions please call me at (301)796-4158 or email: Kofi.Ansah@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

CDR Kofi Ansah, Pharm.D.
Senior Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
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/

KOFI B ANSAH
02/05/2013

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 204150 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type:
Proprietary Name: Established/Proper Name: Desvenlafaxine Extended-Release Dosage Form: 50mg & 100mg Tablets		Applicant: Alembic Pharmaceuticals Limited Agent for Applicant (if applicable): Hari Nagaradona, Ph.D. , Director, Regulatory Affairs; INC Research, LLC , 7361 Calhoun Place, Suite 500, Rockville, MD 20855
RPM: Kofi Ansah, Pharm.D.		Division: Division of Psychiatry Products
<p><u>NDA and NDA Efficacy Supplements:</u></p> <p>NDA Application Type: <input 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)</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><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></p> <p>Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s):</p> <p>NDA 21992 – PRISTIQ (desvenlafaxine) Extended-Release Tablets</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>This current product is the “Desvenlafaxine (base) Extended-Release Tablets</p> <p><input type="checkbox"/> This application does not reply upon a listed drug. <input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input checked="" type="checkbox"/> This application relies on (explain) The Agency’s findings of Safety and Efficacy from the review if the RLD (i.e., PRISTIQ).</p> <p><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft² 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 type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check:</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>December 29, 2012</u> 		<input type="checkbox"/> AP <input checked="" type="checkbox"/> TA <input type="checkbox"/> CR

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.

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).

<ul style="list-style-type: none"> Previous actions (<i>specify type and date for each action taken</i>) 	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> 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 _____ 	<input type="checkbox"/> Received
<ul style="list-style-type: none"> Application Characteristics³ 	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</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> <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> 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> REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Communication Plan <input type="checkbox"/> ETASU <input checked="" type="checkbox"/> MedGuide w/o REMS <input type="checkbox"/> REMS not required </p> <p>Comments:</p>	
<ul style="list-style-type: 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) 	<input type="checkbox"/> Yes, dates
<ul style="list-style-type: none"> BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>) 	<input type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> Public communications (<i>approvals only</i>) 	
<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

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.

❖ Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input type="checkbox"/> No <input checked="" 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 type="checkbox"/> No <input checked="" type="checkbox"/> Yes If yes, NDA # 21992 and date exclusivity expires: 03/01/13
<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 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"/> Not applicable because drug is an old antibiotic.
<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 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 ⁴	12/21/12
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 type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) TA Letter - 12/21/12
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. 	12/20/12
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	02/29/12
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	PRISTIQ Labeling (S-034)

⁴ Fill in blanks with dates of reviews, letters, etc.

<ul style="list-style-type: none"> ❖ 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>) 	<input checked="" type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input 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. 	12/20/12
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	02/29/12
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	PRISTIQ Labeling (S-034)
<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 	11/29/12
<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>) • Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name. 	N/A
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input checked="" type="checkbox"/> RPM 07/17/12 <input checked="" type="checkbox"/> DMEPA 11/04/12 & 12/13/12 <input checked="" type="checkbox"/> DMPP/PLT (DRISK) 11/30/12 <input checked="" type="checkbox"/> ODPD (DDMAC) 12/03/12 (PI & Carton/Container Labels) <input checked="" type="checkbox"/> SEALD <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
<ul style="list-style-type: none"> ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁵/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) 	
<ul style="list-style-type: none"> ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte 	<input type="checkbox"/> Not a (b)(2) TA – 12/05/12
<ul style="list-style-type: none"> ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>) 	<input type="checkbox"/> Not a (b)(2) N/A for TA
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) 	<input type="checkbox"/> Included
<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 checked="" 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 <u>11/14/12</u> If PeRC review not necessary, explain: _____ • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input checked="" type="checkbox"/> Included

⁵ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ 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
❖ Outgoing communications <i>(letters, including response to FDRR (do not include previous action letters in this tab), emails, faxes, telecons)</i>	Included
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• Regulatory Briefing <i>(indicate date of mtg)</i>	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> No mtg
• EOP2 meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) <i>(indicate dates of mtgs)</i>	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 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>	<input type="checkbox"/> None
Cross-Discipline Team Leader Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 12/20/12
PMR/PMC Development Templates <i>(indicate total number)</i>	<input type="checkbox"/> None
Clinical Information⁶	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) <i>(indicate date for each review)</i>	CDTL Review – 12/20/12
• Clinical review(s) <i>(indicate date for each review)</i>	11/28/12
• 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 type="checkbox"/> and include a review/memo explaining why not <i>(indicate date of review/memo)</i>	11/28/12 – See Clinical Review
❖ 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 type="checkbox"/> Not applicable None
❖ Risk Management	
• 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

⁶ Filing reviews should be filed with the discipline reviews.

❖ OSI Clinical Inspection Review Summary(ies) (include copies of OSI letters to investigators)	<input checked="" type="checkbox"/> None requested
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None 11/29/12
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of OSI letters)	<input type="checkbox"/> None 10/09/12 & 04/11/12
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Supervisory Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None 12/10/12
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary (include copies of OSI letters)	<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>		<input type="checkbox"/> None CMC- 11/26/12 (Primary Review); 03/08/12 (Filing Review) Biopharmaceutics - 11/25/12 (Primary Review); 04/24/12 (filing Review)
❖ Microbiology Reviews		<input checked="" type="checkbox"/> Not needed
<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 (OMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>		
❖ 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 type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>		11/26/12 & 03/08/12 (See CMC Review)
<input type="checkbox"/> Review & FONSI <i>(indicate date of review)</i>		
<input type="checkbox"/> Review & Environmental Impact Statement <i>(indicate date of each review)</i>		
❖ Facilities Review/Inspection		
<input type="checkbox"/> NDAs: Facilities inspections (include EER printout) <i>(date completed must be within 2 years of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁷)</i>		Date completed: 09/24/12 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER <i>(date of most recent TB-EER must be within 30 days of action date) (original and supplemental BLAs)</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 type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

⁷ 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.

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy 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).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

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/s/

KOFI B ANSAH
12/21/2012

From: Ansah, Kofi
To: ["Nagaradona, Hari"](#)
Subject: DMEPA Information Request - 2 -- NDA 204150/Desvenlafaxine ER/MDD
Date: Tuesday, December 11, 2012 10:47:00 AM

Dear Hari,

We have the following information request from DMEPA in connection with their review of your Blister Labels.

- Regarding the proposed blister labels, is the product information printed on paper or aluminum foil. Please respond by COB Wednesday, December 12, 2012.
- Additionally, please provide a sample of the 50 mg and 100 mg blister cards containing the proposed blister labels by COB Friday, December 14, 2012.

Best Regards,
Kofi.

Kofi Boadu Ansah, R.Ph., Pharm.D.

CDR, US Public Health Service

Regulatory Project Manager, Division of Psychiatry Products

FDA/Center for Drug Evaluation and Research, Office of Drug Evaluation-I
10903 New Hampshire Avenue, White Oak Bldg 22, Room 4109

Silver Spring, MD 20993 - 0002

Phone: (301) 796-4158

Fax: (301) 796-9838

Email: Kofi.Ansah@fda.hhs.gov

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/s/

KOFI B ANSAH
12/11/2012

From: Ansah, Kofi
To: "Nagaradona, Hari"
Subject: Proposed Labeling (PI &MG) for Revisions & Agreement -- NDA 204150/Desvenlafaxine Extended-Release/ALEMBIC
Date: Saturday, December 08, 2012 3:08:00 PM
Attachments: [12-07-12 PI FDA proposed based on 07-30-12 Sponsor revised draft PI -- NDA 204150 Desvenlafaxine ER.doc](#)
[12-07-12 MG FDA proposed based on 07-30-12 Sponsor revised draft MG -- NDA 204150 Desvenlafaxine ER.doc](#)
Importance: High

Dear Hari,

Attached is our proposed labeling (PI and MG) for your pending NDA 204150. We have made extensive revisions based on your 07/30/12 revised draft labeling. Please review the attached documents and make the requested changes noted below (most of which also appear as comments on the documents) then send the PI and MG back to us with your revisions/comments in track changes.

We need you to make the following changes to the attached labeling:

A) Package Insert (PI):

(i) Return Highlight (HL) to two column format, with ½ inch margins on all sides and in between columns, and align the columns in HL so that they are as close to the same length as possible. Ensure 8 point font is used throughout.

(ii) Ensure horizontal lines appear on both sides of major headings in HL.

(iii) Insert manufacturer's 800-US phone number (and ensure that the toll free # you provide is either a dedicated line or has a prompt that gives an option to speak to someone dedicated to dealing with ADR reporting).

(iv) Insert month/year (at the end of the HL page as indicated) upon application approval.

(v) Revise Table of Contents (TOC) to ensure that the TOC matches the Full Prescribing Information (FPI) with regards to sections and subsections numbers and headings.

(vi) Delete (b) (4)

 Also, delete page number information at the bottom of the page and ensure only one horizontal line separates the TOC from the FPI (Currently, there are 3 lines on this page).

(ii) We have tried to correct the cross references throughout the FPI but please double check to ensure that the cross references are correct and matches your revised TOC.

B) Medication Guide (MG):

(i) Insert the manufacturer's 800-US phone number (see similar comment above).

(iii) Add issued Month/Year to the last page of MG as indicated.

Please effect the requested changes and send us back the revised PI and MG by close-of-business on Wednesday; December 12, 2012. Please indicate in your response whether or not we have agreement on this labeling. You may email me

your response then once we have agreement on labeling, you can formally submit a copy of the agreed upon labeling to your NDA before we take action.

Best Regards,
Kofi.

Kofi Boadu Ansah, R.Ph., Pharm.D.

CDR, US Public Health Service

Regulatory Project Manager, Division of Psychiatry Products

FDA/Center for Drug Evaluation and Research, Office of Drug Evaluation-I
10903 New Hampshire Avenue, White Oak Bldg 22, Room 4109

Silver Spring, MD 20993 - 0002

Phone: (301) 796-4158

Fax: (301) 796-9838

Email: Kofi.Ansah@fda.hhs.gov

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

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/s/

KOFI B ANSAH
12/08/2012



NDA 204150

INFORMATION REQUEST

Alembic Pharmaceuticals Limited
Attention: Hari Nagaradona, Ph.D.
Director, Regulatory Affairs
INC Research, LLC
7361 Calhoun Place, Suite 500
Rockville, MD 20855

Dear Dr. Nagaradona:

Please refer to your New Drug Application (NDA) dated and received February 29, 2012, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Desvenlafaxine Extended-Release Tablets 50 mg and 100 mg.

We also refer to your amendment dated July 30, 2012 which provided your revised proposed labels and labeling (i.e., Package Insert PI), Container & Blister Labels, and Carton Labeling for Blisters).

We have completed our review of your proposed labels and have the following comments for you to implement prior to our taking action on this application.

A. General Comment for All Labels and Labeling:

(b) (4)

These revisions should be made for the labels immediately and revised labels submitted to the NDA for further review, as soon as possible. But you may hold off on revising your proposed PI until you have received our counter-proposal to your PI.

B. Container Labels and Carton Labeling

1. A (b) (4) is used to differentiate the 50 mg strength from the 100 mg strength tablets. However, a (b) (4) is also used to highlight the strength of (b) (4). We note the label of this product may be considered to be different than the (b) (4), but these containers may appear side by side on a pharmacy shelf. This similarity in colors may lead to confusion between these two product strengths. Therefore, consider the use of a different color for the 50 mg strength; one that does not overlap with any of the colors used for (b) (4) strength differentiation. This may help to minimize the potential for confusion.

2. Although the two product strengths are outlined in color, they lack adequate differentiation. Consider expanding the color with the use of a color block as a background for the statement of strength in order to increase prominence and improve differentiation between the product strengths. Ensure adequate contrast between the background colors and the text font color to enhance the readability.
3. Ensure the expiration date format is presented in a manner that is clearly understood (e.g., Month/Day/Year).
4. The medication guide statement lacks prominence. Use a bold font for the statement in order to increase its prominence.

C. Blister Labels

See Comments B.1 and B.2, above and make the same revisions for the Blister Labels.

We request that you resubmit revised labels (i.e., Container/Carton/Blister Labels) that address these issues by December 6, 2012. The resubmitted labeling will be used for further labeling discussions.

If you have any questions, contact CDR Kofi Ansah, Pharm.D., Senior Regulatory Project Manager, at (301)796-4158 or email: Kofi.Ansah@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

THOMAS P LAUGHREN
11/21/2012

Ansah, Kofi

From: Ansah, Kofi
Sent: Saturday, October 27, 2012 6:31 PM
To: 'Nagaradona, Hari'
Subject: Information Request (PEDS Plan) - 2 -- NDA 204150/Desvenlafaxine ER/MDD
Importance: High

Dear Hari:

We acknowledge receipt of your submission, dated and received 10/26/12, in response to our 10/23/12 request for a Pediatric Plan. We note that your response did not include a Pediatric Plan.

We also note that for this application, and at this time, we only intend to grant (i) a Partial-Waiver for patients ages 0-6 years and (ii) Defer Pediatric Studies for patients ages 7-17 years (hence the need for a Peds Plan).

We again request that you provide a Pediatric Plan. Your pediatric plan must contain elements that will allow the Agency to determine whether the plan is sufficient to provide adequate data for dosing, safety, and efficacy for use in the appropriate pediatric populations. A synopsis of your proposed studies is to include the final report submission date as well as the relevant age ranges to be studied [also refer to our email below from 10/23/12].

Please provide the requested information as soon as possible but preferably no later than close-of-business on Wednesday; 10/31/12.

Best Regards,
Kofi.

From: Nagaradona, Hari [mailto:Hari.Nagaradona@INCRsearch.com]
Sent: Friday, October 26, 2012 11:29 AM
To: Ansah, Kofi
Subject: RE: Information Request (PEDS Plan) -- NDA 204150/Desvenlafaxine ER/MDD

Dear Kofi

We submitted the response to your query through gateway.. I am also forwarding the same by email for your reference. Please let me know if you have any questions.

Thanks and Best regards,

Hari

Hari Nagaradona, PhD | Director, Regulatory Affairs | Regulatory Strategy, Consulting and Submissions
INC Research, LLC
7361 Calhoun Place, Suite 500, Rockville, MD 20855 | USA
Tel: +1-301-296-1370 | Mobile: (b) (6) Fax: +1-301-838-3182
hari.nagaradona@incresearch.com | www.incresearch.com | **INC Research®**

From: Ansah, Kofi [mailto:Kofi.Ansah@fda.hhs.gov]
Sent: Tuesday, October 23, 2012 10:16 AM
To: Nagaradona, Hari
Subject: Information Request (PEDS Plan) -- NDA 204150/Desvenlafaxine ER/MDD
Importance: High

Dear Hari,

Regarding your NDA currently under review, we need you to provide the following information.

REQUIRED PEDIATRIC ASSESSMENTS

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

A draft guidance on the implementation of PREA was issued by FDA in September 2005 and is available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079756.pdf>.

As such, a pediatric plan needs to be submitted to address this NDA.

Your pediatric plans must contain elements that will allow the Agency to determine whether the plan is sufficient to provide adequate data for dosing, safety, and efficacy for use in the appropriate pediatric populations. A synopsis of your proposed studies is to include the final report submission date as well as the relevant age ranges to be studied.

All requests for pediatric waivers must include a scientific rationale to support the waiver request.

Please amend your application within 2 weeks to address this deficiency.

Best Regards,
Kofi.

Kofi Boadu Ansah, R.Ph., Pharm.D.

CDR, US Public Health Service
Regulatory Project Manager, Division of Psychiatry Products
FDA/Center for Drug Evaluation and Research, Office of Drug Evaluation-I
10903 New Hampshire Avenue, White Oak Bldg 22, Room 4109
Silver Spring, MD 20993 - 0002
Phone: (301) 796-4158
Fax: (301) 796-9838

Email: Kofi.Ansah@fda.hhs.gov

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/s/

KOFI B ANSAH
10/31/2012

From: Ansah, Kofi
To: ["Nagaradona, Hari"](#)
Cc: [Griffith, Sandra J](#)
Subject: DMEPA Information Request -- NDA 204150/Desvenlafaxine ER/MDD
Date: Friday, September 14, 2012 5:37:00 PM

Dear Dr. Nagaradona,

Regarding your NDA currently under review, DMEPA is in the process of reviewing the label and labeling for this product and has the following request for clarification. You are proposing multiple bottle sizes which includes a 14-count bottle but the label for the 14-count size doesn't state "Professional Sample". DMEPA would like to know whether it is a professional sample or not ?

Please provide your response to the requested information as soon as possible.

Thanks,
Kofi.

Kofi Boadu Ansah, R.Ph., Pharm.D.

CDR, US Public Health Service

Regulatory Project Manager, Division of Psychiatry Products

FDA/Center for Drug Evaluation and Research, Office of Drug Evaluation-I
10903 New Hampshire Avenue, White Oak Bldg 22, Room 4109

Silver Spring, MD 20993 - 0002

Phone: (301) 796-4158

Fax: (301) 796-9838

Email: Kofi.Ansah@fda.hhs.gov

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/s/

KOFI B ANSAH
09/14/2012



NDA 204150

INFORMATION REQUEST

Alembic Pharmaceuticals Limited
c/o INC Research, LLC, Authorized U.S. Agent
Attention: Hari Nagaradona, Ph.D.
Director, Regulatory Affairs
7361 Calhoun Place, Suite 500
Rockville, MD 20855

Dear Dr. Nagaradona:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Desvenlafaxine (Base) Extended-Release Tablets 50 mg and 100 mg.

We are reviewing the Chemistry, Manufacturing and Controls sections of your submission and have the following comments and information requests. We request a written response by August 31, 2012, in order to continue our evaluation of your NDA.

1. Revise your post-approval stability commitment by including a commitment to perform stability studies on the first three commercial lots of desvenlafaxine (base) extended-release tablets 50 mg and 100 mg tablets under both long-term storage conditions as well as accelerated storage conditions.
2. Include microbiological testing in drug product specification or provide justification, with supporting data, for excluding microbiological testing from proposed drug product specification.
3. Given that the Impurity (b) (4) is either undetectable or present at levels of \leq (b) (4) in the drug product and stability batches, your proposed acceptance limit of (b) (4) for the Impurity (b) (4) is not supported by batch analysis data. Tighten the acceptance limit for Impurity (b) (4) to the level that is supported by your batch analysis data.
4. We have issued a DMF deficiency letter to the holder of Type II DMF 25527, dated August 7, 2012. Approval of the NDA is contingent upon adequate information being provided in a supporting DMF.

If you have any questions, contact Teshara G. Bouie, Regulatory Project Manager, at (301) 796-1649.

Sincerely,

{See appended electronic signature page}

Ramesh Sood, Ph.D.
Branch Chief
Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

RAMESH K SOOD
08/07/2012



NDA 204150

INFORMATION REQUEST

Alembic Pharmaceuticals Limited
Attention: Hari Nagaradona, Ph.D.
Director, Regulatory Affairs
INC Research, LLC
7361 Calhoun Place, Suite 500
Rockville, MD 20855

Dear Dr. Nagaradona:

Please refer to your New Drug Application (NDA) dated and received February 29, 2012, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Desvenlafaxine (Base) Extended-Release Tablets 50 mg and 100 mg.

During our preliminary review of your submitted labeling, we have identified the following labeling format issues:

Highlights (HL)

1. The HL must be less than or equal to one-half page. Please request a waiver for this requirement if you haven't already done so.
2. The HL Limitation Statement must be on the line immediately beneath the HL heading.
3. Initial U.S. Approval must be placed immediately beneath the product title.
4. The Boxed Warning (BW) heading needs to be centered.
5. You included the verbatim statement "See full prescribing information for complete boxed warning" but this statement must be centered and placed immediately beneath the BW heading.
6. For drug products other than vaccines, the verbatim **bolded** statement, "**To report SUSPECTED ADVERSE REACTIONS, contact (insert name of manufacturer) at (insert manufacturer's phone number) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch**" must be present.

We note that you did include this statement except that the manufacturer portion is missing. Please include the manufacturer's name and US phone # (i.e., 800-#) as indicated.

7. For the Patient Counseling Information Statement, please use the following bolded verbatim statement (without the quotation marks): "**See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.**"
8. **Revision Date:** Please insert a place-holder date presented as MM/YYYY or Month/Year to be replaced by month/year of the application approval.

Full Prescribing Information (FPI)

9. The **bolded** section and subsection headings must be named and numbered in accordance with 21 CFR 201.56(d)(1) as noted below. If a section/subsection is omitted, the numbering does not change. For e.g., 12.4 and 12.5 should be Microbiology and Pharmacogenomics, respectively, by guidance. If omitted the numbering does not change.
10. **Patient Counseling Information** must reference any FDA-approved patient labeling, include the type of patient labeling, and use the following statement at the beginning of Section 17: “See FDA-approved patient labeling (Medication Guide)”

Additionally, please remove the header and footer from your proposed labeling.

We request that you resubmit labeling that addresses these issues by August 6, 2012. The resubmitted labeling will be used for further labeling discussions.

If you have any questions, contact CDR Kofi Ansah, Pharm.D., Senior Regulatory Project Manager, at (301)796-4158 or email: Kofi.Ansah@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

MITCHELL V Mathis
07/17/2012
For Dr. Laughren

From: [Ansah, Kofi](#)
To: ["Nagaradona, Hari"](#)
Subject: OCP Info Request -- NDA 204150/Desvenlafaxine (Bas) ER/MDD
Date: Tuesday, July 10, 2012 6:09:00 PM

Dear Dr. Nagaradona,

Regarding your NDA currently under review, please provide the SAS code used in the statistical analysis for the BE studies. Include in your submission/response the code for the 90% confidence interval determination. Please provide your response as soon as possible.

Best Regards,
Kofi.

Kofi Boadu Ansah, R.Ph., Pharm.D.

CDR, US Public Health Service

Regulatory Project Manager, Division of Psychiatry Products

FDA/Center for Drug Evaluation and Research, Office of Drug Evaluation-I
10903 New Hampshire Avenue, White Oak Bldg 22, Room 4109

Silver Spring, MD 20993 - 0002

Phone: (301) 796-4158

Fax: (301) 796-9838

Email: Kofi.Ansah@fda.hhs.gov

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/s/

KOFI B ANSAH
07/10/2012



NDA 204150

FILING COMMUNICATION

Alembic Pharmaceuticals Limited
Attention: Hari Nagaradona, Ph.D.
Director, Regulatory Affairs
INC Research, LLC
7361 Calhoun Place, Suite 500
Rockville, MD 20855

Dear Dr. Nagaradona:

Please refer to your New Drug Application (NDA) dated and received February 29, 2012, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Desvenlafaxine (Base) Extended-Release Tablets 50 mg and 100 mg.

We also refer to your amendments dated March 12, 2012.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is December 29, 2012.

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 includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team 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 December 8, 2012.

At this time, we are notifying you that, we have not identified any potential review issues. 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.

We request that you submit the following information:

1. Please evaluate the alcohol induced dose dumping of your product.
 - Dissolution testing should be conducted using the optimal dissolution apparatus and agitation speed. Dissolution data should be generated from 12 dosage units (n=12) at multiple time points to obtain a complete dissolution profile.
 - The following alcohol concentrations for the in vitro dissolution studies are recommended: 0%, 5%, 10%, 20%, and 40%.
 - Dissolution profiles using the above range of alcohol concentrations in three physiologically relevant pH media (pH 1.2, 4.5, and 6.8) are recommended.
 - The shape of the dissolution profiles should be compared to determine if the modified release characteristics are maintained, especially in the first 2 hours.
 - The f2 values assessing the similarity (or lack thereof) between the dissolution profiles should be estimated (using 0% alcohol as the reference).
 - The report with the complete data (i.e., individual, mean, SD, comparison plots, f2 values, etc.) collected during the evaluation of the in vitro alcohol induced dose dumping study should be provided to FDA for review and comments.
2. The proposed dissolution acceptance criteria for the dissolution test need to be revised. Specifically, the following is recommended; 1) to set an acceptance range for the 1 h time point, based on the data provided, we recommend a range of (b) (4); 2) to tighten the acceptance range to (b) (4) for the 8 h time point. We recommend a range of (b) (4), based on the data provided; and 3) to provide additional dissolution data at 10, 12, and 16 hours time points, to explore the possibility of setting (b) (4) at a time point earlier than 20 h.
3. Please submit a correctly worded Debarment Certification to the NDA. Given that the sponsor is a foreign applicant, both the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications]. Debarment Certification should use wording in FDCA Section 306(k)(1) i.e., “[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.”

Please respond only to the above requests for information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission. We request that you provide the requested information by **June 30, 2012**.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form

with annotated references, and the proposed package insert (PI), Medication Guide, and patient PI (as applicable). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

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

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), and Medication Guide, and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

REQUIRED PEDIATRIC ASSESSMENTS

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

We note that you have not addressed how you plan to fulfill this requirement. Within 30 days of the date of this letter, please submit (1) a full waiver request, (2) a partial waiver request and a pediatric development plan for the pediatric age groups not covered by the partial waiver request, or (3) a pediatric drug development plan covering the full pediatric age range. All waiver requests must include supporting information and documentation. A pediatric drug development plan must address the indication proposed in this application.

If you request a full waiver, we will notify you if the full waiver is denied and a pediatric drug development plan is required.

Pediatric studies conducted under the terms of section 505B of the Federal Food, Drug, and Cosmetic Act (the Act) may also qualify for pediatric exclusivity under the terms of section 505A of the Act. If you wish to qualify for pediatric exclusivity please consult Division of Psychiatry Products. Please note that satisfaction of the requirements in section 505B of the Act alone may not qualify you for pediatric exclusivity under 505A of the Act.

If you have any questions, contact CDR Kofi Ansah, Pharm.D., Senior Regulatory Project Manager, at (301)796-4158 or email: Kofi.Ansah@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
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/

THOMAS P LAUGHREN
05/11/2012



NDA 204150

NDA ACKNOWLEDGMENT

Alembic Pharmaceuticals Limited
Attention: Hari Nagaradona, Ph.D.
Director, Regulatory Affairs
INC Research, LLC
7361 Calhoun Place, Suite 500
Rockville, MD 20855

Dear Dr. Nagaradona:

We have received your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Desvenlafaxine (Base) Extended-Release Tablets 50 mg and 100 mg

Date of Application: February 29, 2012

Date of Receipt: February 29, 2012

Our Reference Number: NDA 204150

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 April 29, 2012, 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/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. 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.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

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 Psychiatry 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/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

If you have any questions please call me at (301)796-4158 or email: Kofi.Ansah@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

CDR Kofi Ansah, Pharm.D.
Senior Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

KOFI B ANSAH
04/02/2012