

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**203696Orig1s000**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

## EXCLUSIVITY SUMMARY

NDA # 203696

SUPPL #

HFD # 580

Trade Name LUPANETA PACK

Generic Name (leuprolide acetate for depot suspension; norethindrone acetate tablets)

Applicant Name Abbott Endocrine, Inc.

Approval Date, If Known 12-14-2012

### 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)(1)

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

YES  NO

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

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

d) Did the applicant request exclusivity?

YES  NO

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

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

YES  NO

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

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

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

YES  NO

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

## **PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES**

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES  NO

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

NDA#

NDA#

NDA#

2. Combination product.

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

YES  NO

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

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:





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: Kim Shiley  
Title: Regulatory Health Project Manager  
Date: December 10, 2012

Name of Office/Division Director signing form: Audrey Gassman, M.D.  
Title: Deputy Director

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/  
-----

KIMBERLY A SHILEY  
12/14/2012

AUDREY L GASSMAN  
12/14/2012



### **1.3.3 Debarment Certification**

#### **Certification Requirement for Approval of a Drug Product(s) Concerning Using Services of Debarred Persons**

Any applicant for approval of a new drug product submitted on or after June 1, 1992 per Section 306(k)(1) of the Federal Food, Drug, and Cosmetic Act must include:

- (1) A certification that the applicant did not and will not use in any capacity the services of any person debarred under Section 306, subsection (a) and (b), in connection with such application.

Abbott Laboratories certifies that it did not, and will not use in any capacity the services of any person debarred under Section 306, subsection (a) and (b), in connection with this application.

[See attached electronic signature]

Jean M. Conaway, RPh, RAC, MBA  
Associate Director, Regulatory Affairs - PPG  
Abbott Endocrine Inc., a wholly owned subsidiary of Abbott Laboratories

## Document Approval

Debarment Certification - 2011-dec-15

Version: 1.0

Date: 24-Nov-2011 04:05:44 AM Abbott ID: 11242011-00AB61A0094290-00001-en

<b>Signed by:</b> Conaway_Jean_M	<b>Date:</b> 24-Nov-2011 04:05:41 AM	<b>Meaning Of Signature:</b> Approver
-------------------------------------	---	--

# ACTION PACKAGE CHECKLIST

## APPLICATION INFORMATION<sup>1</sup>

NDA # 203696	NDA Supplement # n/a	If NDA, Efficacy Supplement Type:
Proprietary Name: LUPANETA PACK Established/Proper Name: leuprolide acetate for depot suspension and norethindrone acetate tablets Dosage Form: depot suspension given as an intramuscular injection, tablets		Applicant: Abbott Endocrine, Inc. Agent for Applicant (if applicable):
RPM: Shiley		Division: Division of Reproductive and Urologic Products
<b><u>NDAs and NDA Efficacy Supplements:</u></b>  NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)  (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.)		<b><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></b>  Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):  Provide a brief explanation of how this product is different from the listed drug.  <input type="checkbox"/> This application does not rely upon a listed drug. <input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> This application relies on (explain)  <b><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft<sup>2</sup> to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></b>  <b><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></b>  <input type="checkbox"/> No changes <input type="checkbox"/> Updated    Date of check:
❖ Actions		
<ul style="list-style-type: none"> <li>• Proposed action</li> <li>• User Fee Goal Date is <u>December 15, 2012</u></li> </ul>		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> <li>• Previous actions (<i>specify type and date for each action taken</i>)</li> </ul>		<input checked="" type="checkbox"/> None

<sup>1</sup> 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.

<sup>2</sup> 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).

<p>❖ 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 <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf</a>). If not submitted, explain _____</p>	<p><input type="checkbox"/> Received</p>
<p>❖ Application Characteristics <sup>3</sup></p> <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 <span style="margin-left: 200px;">BLAs: Subpart E</span>  <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <span style="margin-left: 100px;"><input type="checkbox"/> Accelerated approval (21 CFR 601.41)</span>  <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <span style="margin-left: 100px;"><input type="checkbox"/> Restricted distribution (21 CFR 601.42)</span></p> <p>Subpart I <span style="margin-left: 200px;">Subpart H</span>  <input type="checkbox"/> Approval based on animal studies <span style="margin-left: 100px;"><input type="checkbox"/> Approval based on animal studies</span></p> <p><input type="checkbox"/> Submitted in response to a PMR <span style="margin-left: 200px;">REMS: <input type="checkbox"/> MedGuide</span>  <input type="checkbox"/> Submitted in response to a PMC <span style="margin-left: 100px;"><input type="checkbox"/> Communication Plan</span>  <input type="checkbox"/> Submitted in response to a Pediatric Written Request <span style="margin-left: 100px;"><input type="checkbox"/> ETASU</span>  <span style="margin-left: 400px;"><input type="checkbox"/> MedGuide w/o REMS</span>  <span style="margin-left: 400px;"><input type="checkbox"/> REMS not required</span></p> <p>Comments:</p>	
<p>❖ 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)</p>	<p><input type="checkbox"/> Yes, dates</p>
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> <li>• Office of Executive Programs (OEP) liaison has been notified of action</li> </ul>	<p><input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>
<ul style="list-style-type: none"> <li>• Press Office notified of action (by OEP)</li> </ul>	<p><input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>
<ul style="list-style-type: none"> <li>• Indicate what types (if any) of information dissemination are anticipated</li> </ul>	<p><input checked="" type="checkbox"/> None  <input type="checkbox"/> HHS Press Release  <input type="checkbox"/> FDA Talk Paper  <input type="checkbox"/> CDER Q&amp;As  <input type="checkbox"/> Other</p>

<sup>3</sup> 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"> <li>Is approval of this application blocked by any type of exclusivity?</li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> <li>NDA and BLA: 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></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(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></li> </ul>	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(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></li> </ul>	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(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></li> </ul>	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>NDA 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></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date 10-year limitation expires: _____
<b>❖ Patent Information (NDAs only)</b>	
<ul style="list-style-type: none"> <li>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.</li> </ul>	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> <li>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.</li> </ul>	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> <li>[505(b)(2) applications] If the application includes a <b>paragraph III</b> 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).</li> </ul>	<input type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> <li>[505(b)(2) applications] For <b>each paragraph IV</b> 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></li> </ul>	<input type="checkbox"/> N/A (no paragraph IV certification) <input 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>	<p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p>
---	--

**CONTENTS OF ACTION PACKAGE**

❖ Copy of this Action Package Checklist <sup>4</sup>	
<b>Officer/Employee List</b>	
❖ 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
<b>Action Letters</b>	
❖ Copies of all action letters ( <i>including approval letter with final labeling</i> )	Action(s) and date(s) 12-14-2012
<b>Labeling</b>	
❖ Package Insert ( <i>write submission/communication date at upper right of first page of PI</i> )	
<ul style="list-style-type: none"> <li>• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	12-14-2012 (division) 1213-2012 (sponsor)
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	2-15-2012
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	n/a

<sup>4</sup> Fill in blanks with dates of reviews, letters, etc.

<ul style="list-style-type: none"> <li>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>)</li> </ul>	<input type="checkbox"/> Medication Guide <input checked="" 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"> <li>Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	12-14-2012 (division) 12-12-2012 (sponsor)
<ul style="list-style-type: none"> <li>Original applicant-proposed labeling</li> </ul>	11-16-2012
<ul style="list-style-type: none"> <li>Example of class labeling, if applicable</li> </ul>	
<ul style="list-style-type: none"> <li>❖ Labels (<b>full color</b> carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)</li> </ul>	
<ul style="list-style-type: none"> <li>Most-recent draft labeling</li> </ul>	12-6-2012 12-11-2012
<ul style="list-style-type: none"> <li>❖ Proprietary Name               <ul style="list-style-type: none"> <li>Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)</li> <li>Review(s) (<i>indicate date(s)</i>)</li> <li>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.</li> </ul> </li> </ul>	11-02-2012 Acceptable 10-25-2012
<ul style="list-style-type: none"> <li>❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)</li> </ul>	<input checked="" type="checkbox"/> RPM 4-26-2012 <input checked="" type="checkbox"/> DMEPA 7-20- & 10-31-2012 <input checked="" type="checkbox"/> DMPP/PLT (DRISK) 11-28-2012 <input checked="" type="checkbox"/> ODPD (DDMAC) 12-3-2012 <input checked="" type="checkbox"/> SEALD 12-14-2012 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
<b>Administrative / Regulatory Documents</b>	
<ul style="list-style-type: none"> <li>❖ Administrative Reviews (<i>e.g., RPM Filing Review<sup>5</sup>/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)</li> </ul>	April 13, 2012
<ul style="list-style-type: none"> <li>❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte</li> </ul>	<input type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> <li>❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>)</li> </ul>	<input type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> <li>❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)</li> </ul>	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> <li>❖ Application Integrity Policy (AIP) Status and Related Documents <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a></li> </ul>	
<ul style="list-style-type: none"> <li>Applicant is on the AIP</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>This application is on the AIP               <ul style="list-style-type: none"> <li>If yes, Center Director's Exception for Review memo (<i>indicate date</i>)</li> <li>If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No  <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> <li>❖ Pediatrics (<i>approvals only</i>)               <ul style="list-style-type: none"> <li>Date reviewed by PeRC</li> <li>If PeRC review not necessary, explain: <u>co-packaged product</u></li> <li>Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>)</li> </ul> </li> </ul>	Does not trigger  <input type="checkbox"/> Included

<sup>5</sup> 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>	
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
<ul style="list-style-type: none"> <li>• Regulatory Briefing <i>(indicate date of mtg)</i></li> </ul>	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> <li>• If not the first review cycle, any end-of-review meeting <i>(indicate date of mtg)</i></li> </ul>	<input checked="" type="checkbox"/> N/A or no mtg
<ul style="list-style-type: none"> <li>• Pre-NDA/BLA meeting <i>(indicate date of mtg)</i></li> </ul>	<input type="checkbox"/> No mtg 11-10-2011
<ul style="list-style-type: none"> <li>• EOP2 meeting <i>(indicate date of mtg)</i></li> </ul>	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> <li>• Other milestone meetings (e.g., EOP2a, CMC pilots) <i>(indicate dates of mtgs)</i></li> </ul>	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
<ul style="list-style-type: none"> <li>• Date(s) of Meeting(s)</li> </ul>	
<ul style="list-style-type: none"> <li>• 48-hour alert or minutes, if available <i>(do not include transcript)</i></li> </ul>	
<b>Decisional and Summary Memos</b>	
❖ 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 12-14-2012
Cross-Discipline Team Leader Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 12-13-2012
PMR/PMC Development Templates <i>(indicate total number)</i>	<input checked="" type="checkbox"/> None
<b>Clinical Information<sup>6</sup></b>	
❖ Clinical Reviews	
<ul style="list-style-type: none"> <li>• Clinical Team Leader Review(s) <i>(indicate date for each review)</i></li> </ul>	11-15-2012; 4-12-2012
<ul style="list-style-type: none"> <li>• Clinical review(s) <i>(indicate date for each review)</i></li> </ul>	11-15-2012; 4-12-2012
<ul style="list-style-type: none"> <li>• Social scientist review(s) (if OTC drug) <i>(indicate date for each review)</i></li> </ul>	<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>	See Clinical Review, 11-15-2012, page 11
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management	
<ul style="list-style-type: none"> <li>• REMS Documents and Supporting Statement <i>(indicate date(s) of submission(s))</i></li> <li>• REMS Memo(s) and letter(s) <i>(indicate date(s))</i></li> <li>• 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></li> </ul>	<input checked="" type="checkbox"/> None

<sup>6</sup> Filing reviews should be filed with the discipline reviews.

❖ DSI Clinical Inspection Review Summary(ies) (include copies of DSI letters to investigators)	<input checked="" type="checkbox"/> None requested
<b>Clinical Microbiology</b> <input checked="" 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
<b>Biostatistics</b> <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 type="checkbox"/> None 11-15-2012; 4-26-2012
Statistical Review(s) (indicate date for each review)	<input type="checkbox"/> None 11-15-2012; 4-16-2012
<b>Clinical Pharmacology</b> <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 type="checkbox"/> None 11-15-2012; 4-13-2012
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None 11-15-2012; 4-13-2012
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)	<input checked="" type="checkbox"/> None
<b>Nonclinical</b> <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 type="checkbox"/> None 5-7-2012; 4-6-2012
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None 5-7-2012; 4-6-2012
❖ 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
❖ DSI Nonclinical Inspection Review Summary (include copies of DSI letters)	<input checked="" type="checkbox"/> None requested
<b>Product Quality</b> <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None 10-2-2012; 4-13-2012
• Product quality review(s) including ONDQA biopharmaceutics reviews (indicate date for each review)	<input type="checkbox"/> None 10-2-2012; 4-13-2012
❖ Microbiology Reviews	<input checked="" type="checkbox"/> Not needed
<input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (indicate date of each review)	
<input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) (indicate date of each review)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)	<input checked="" type="checkbox"/> None

Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion ( <i>indicate review date</i> )( <i>all original applications and all efficacy supplements that could increase the patient population</i> )	See Product Quality Discipline Review, dated 10-2-2012, page 24
<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</i> ) ( <i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites<sup>7</sup></i> )	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input checked="" 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</i> ) ( <i>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)

<sup>7</sup> 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.



NDA 203696

**INFORMATION REQUEST**

---

**From:** Shiley, Kimberly  
**Sent:** Friday, November 02, 2012 5:40 PM  
**To:** 'Koev, Gennadiy'  
**Subject:** NDA 203696, information request

Greetings Gennadiy,

We are reviewing the product labeling and are requesting that you develop a Patient Package Insert (PPI) for your product. Reference 21 CFR 208.20, Content and Format of a Medication Guide, although you will be developing a PPI, NOT a medication guide. Additionally, as a model for form, we suggest that you refer to the Mirena PPI approved October 1, 2009 (you can access this on [Drugs@FDA](mailto:Drugs@FDA)). Do not incorporate the specific content, just the format, provided in the Mirena PPI. Discuss both components of your product at a high level; you do not need to diagram the syringe, etc. because the leuprolide acetate component is administered in the healthcare provider's office. The following points should be addressed, along with any other proposed additional topics you believe important to patient understanding. Do not include any information that is not discussed in the Prescribing Information (PI), and not everything in the PI needs to be covered in the PPI. Please submit the draft PPI by November 16, 2012.

- What is Lupaneta Pack?
- What is Lupaneta Pack used for?
- How does Lupaneta Pack work? [discuss each component]
- How well does Lupaneta Pack work? [provide efficacy data from Section 14 of the PI for the combined product]
- Who should not use Lupaneta Pack?
- Before using Lupaneta Pack, tell your provider...
- How is Lupaneta Pack administered? [discuss injection done by HCP and tablets dosed orally on a daily basis by the patient]
- What if I become pregnant?
- What are the possible side effects of Lupaneta Pack?
- While using Lupaneta Pack, when should I call my healthcare provider?
- General advice about prescription medicines.

Additionally, attached is a courtesy copy of a General Advice Letter regarding carton and container labeling that went out in the mail today. I left off the street address and am concerned it may not reach you via USPS.



General Advice  
Letter NDA 2036...

**Kim Shiley, RN, BSN, BSBA**  
Regulatory Health Project Manager  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

NDA 203696

Page 2

Bldg 22, Room 5377

office: 301-796-2117

fax: 301-796-9897

[kimberly.shiley@fda.hhs.gov](mailto:kimberly.shiley@fda.hhs.gov)

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

/s/  
-----

KIMBERLY A SHILEY  
11/06/2012



NDA 203696

**INFORMATION REQUEST**

---

**From:** Shiley, Kimberly  
**Sent:** Tuesday, November 06, 2012 1:58 PM  
**To:** 'Koev, Gennadiy'  
**Cc:** Kober, Margaret  
**Subject:** RE: NDA 203696, information request

Hi again Gennadiy,

Lupaneta Pack should be reserved for instances in which you refer to the entire kit, including both components. If only talking about the leuprolide acetate component, refer to it as leuprolide acetate for depot suspension.

As far as Q1:

Please advise us on whether we can continue to use the name (b) (4) on the syringe and the container labels of the Lupron component of the kit, or if the labels on the syringe and the clamshell should be revised:

We would like to get back to you on this after some internal discussion.

Also, should the tradename Lupaneta Pack be prominently displayed on the norethindrone acetate container label, preceding the established name?

The answer is no, Lupaneta Pack should appear only on the carton labeling that contains both components. The Norethindrone container label should say Norethindrone.

Does this mean that this tradename is acceptable to the Agency, and should we update the USPI replacing TRADENAME with LUPANETA PACK?

The name is acceptable but please do not submit anything new prior to 11/15; we will have revised labeling to you by then. Insert the tradename when you respond to our labeling revisions and comments.

Kim Shiley, RN, BSN, BSBA  
Regulatory Health Project Manager  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research  
10903 New Hampshire Avenue  
Silver Spring, MD 20993  
Bldg 22, Room 5377  
office: 301-796-2117  
fax: 301-796-9897  
kimberly.shiley@fda.hhs.gov

---

**From:** Koev, Gennadiy [mailto:gennadiy.koev@abbott.com]  
**Sent:** Monday, November 05, 2012 4:44 PM  
**To:** Shiley, Kimberly  
**Subject:** RE: NDA 203696, information request

Dear Kim,

We have started to address Agency's comments you provided to me last Friday. Based on the General Advice document you attached, I have two questions regarding the names of the copack and the individual components:



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

/s/  
-----

KIMBERLY A SHILEY  
11/06/2012



NDA 203696

**PROPRIETARY NAME REQUEST  
WITHDRAWN**

Abbott Endocrine Inc.  
200 Abbott Park Road  
Dept PA77/Bldg. AP30-1  
Abbott Park, Illinois 60064-6157

ATTENTION: Gennadiy Koev, Ph.D.  
Manager, RA-PPG

Dear Dr. Koev:

Please refer to your New Drug Application (NDA) dated February 15, 2012, received February 15, 2012, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Leuprolide Acetate for Depot Suspension and Norethindrone Acetate Tablets Co-packaged kits, 3.75 mg/5 mg and 11.25 mg/5 mg.

We acknowledge receipt of your correspondence, dated and received October 02, 2012, notifying us that you are withdrawing your July 10, 2012, request for a review of the proposed proprietary name [REDACTED] (b) (4). This proposed proprietary name request is considered withdrawn as of October 02, 2012.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Marcus Cato, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3903. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Kim Shiley at (301)796-2117.

Sincerely,

*{See appended electronic signature page}*

Carol Holquist, RPh  
Director  
Division of Medication Error Prevention and Analysis  
Office of Medication Error Prevention and Risk Management  
Office of Surveillance and Epidemiology  
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/  
-----

CAROL A HOLQUIST  
11/02/2012



NDA 203696

**PROPRIETARY NAME REQUEST  
CONDITIONALLY ACCEPTABLE**

Abbott Endocrine Inc.  
200 Abbott Park Road  
Dept PA77/Bldg. AP30-1  
Abbott Park, Illinois 60064-6157

ATTENTION: Gennadiy Koev, Ph.D.  
Manager, RA-PPG

Dear Dr. Koev:

Please refer to your New Drug Application (NDA) dated February 15, 2012, received February 15, 2012, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Leuprolide Acetate for Depot Suspension and Norethindrone Acetate Tablets Co-packaged kits, 3.75 mg/5 mg and 11.25 mg/5 mg.

We also refer to your correspondence, dated and received October 02, 2012, requesting review of your proposed proprietary name, Lupaneta Pack. We have completed our review of the proposed proprietary name, Lupaneta Pack and have concluded that it is acceptable.

We have completed our review of the proposed proprietary name, Lupaneta Pack, and have concluded that it is acceptable.

The proposed proprietary name, Lupaneta Pack, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your October 02, 2012, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Marcus Cato, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3903. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Kim Shiley at (301)796-2117.

Sincerely,

*{See appended electronic signature page}*

Carol Holquist, RPh  
Director  
Division of Medication Error Prevention and Analysis  
Office of Medication Error Prevention and Risk Management  
Office of Surveillance and Epidemiology  
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/  
-----

CAROL A HOLQUIST  
11/02/2012



NDA 203696

**GENERAL ADVICE**

Abbott Endocrine, Inc.  
Attention: Gennadiy Koev, Ph.D.  
Manager, Regulatory Affairs – PPG  
Dept. PA77, Bldg. AP30  
Abbott Park, IL 60064-6157

Dear Dr. Koev:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for leuprolide acetate for depot suspension and norethindrone acetate tablets.

We also refer to your September 24, 2012, submission containing carton and container labeling.

We have reviewed the referenced material and have the following recommendations:

**Norethindrone Acetate Tablets Container Labels**

Revise the usual dosage statement “See Package Insert for full prescribing information” to state the actual dose of the product (i.e., “Take 5 mg (1 tablet) by mouth once daily for 30 days” or “Take 5 mg (1 tablet) by mouth once daily for 90 days”). Because this product comes in a large carton, pharmacists may label the carton and not open the carton to place a pharmacy label on the individual components of the pack. Additionally, patients may throw away this large carton after the Lupron component has been administered to save space in their home. Revising the usual dose statement on the Norethindrone Acetate tablets will ensure that the patients have directions for the tablets even if they discard the carton.

**Lupron Component**

Based upon postmarketing errors with the Lupron product line and analysis of the proposed labels and labeling for Lupron Depot and Lupaneta Pack labeling, we recommend the following to be implemented prior to approval of this NDA. Additionally, we recommend that these changes also be carried across your entire Lupron product line at the time of next printing:

A. *Container Labels*

Lupron Depot syringe (3.75 mg and 11.25 mg)

- a. Relocate the established name to appear directly under the name, Lupron Depot, followed by the product strength, and frequency of administration on the Lupron Depot syringe. The revised presentation should appear as follows (note the use of title case lettering):

### **Lupron Depot**

(leuprolide acetate for depot suspension)

3.75 mg (or 11.25 mg)

For 1-month (or 3-month) administration

#### **For intramuscular injection**

- b. Remove the color block currently used for the NDC number and product description and use it to present the strength and the frequency of administration (see the presentation above). Additionally, use a lighter color purple for the 3.75 mg strength to increase the visual contrast between the color block and the black font of the text.
  - c. Include the route of administration, ‘For intramuscular injection’ on the principal display panel of the Lupron Depot syringe label (see the presentation above). This information can be placed under the color block containing the product strength and the frequency of administration, in bold letters.
- B. Clam shell Carton Labeling (3.75 mg/5 mg and 11.25 mg/5 mg)*
1. Present the established name in parenthesis, followed by the product strength, the frequency of administration, and the route of administration (see the presentation in A1).
  2. Box the strength statement and the frequency of administration with the same color band that is used for each strength and frequency of administration at the top of the clam shell labeling to increase visual differentiation between the 3.75 mg and 11.25 mg strengths. The strength and frequency statement should also be bolded. Although the color differentiation between the two strengths of Lupron Depot kits placed inside of the proposed outer carton may not be as critical for the proposed product, for the purpose of consistency, the changes in the presentation of information should be implemented in all the available Lupron products.
  3. Revise the interior of the clam shell labeling to include a warning or statement that alerts practitioners to the correct patient population and frequency of administration on the inside of the clam shell. If a pharmacy label covers the population recommendations provided by the pictures on the principal display panel of the carton and clam shell labeling, the practitioner who is administering the drug may see this information when the clam shell is opened.
  4. (b) (4) “ Not made with natural rubber latex”.
  5. Retain the inactive ingredient statement on the principal display panel. We realize in previous communications you were instructed that the inactive ingredient statement could be deleted. However, this recommendation was not correct and this statement should remain on the carton labeling. This inactive ingredient information can be reformatted, made smaller, and relocated to the bottom right of the labeling where (b) (4), “Rx Only”, and the Abbott symbol are currently located to help include the inactive ingredient information on the labeling of the principal display panel.
  6. Relocate the “Rx only” symbol and reduce its prominence to help make room for required labeling statements on the labeling.

7. Relocate or delete the Abbott logo to help make room for required labeling statements.
8. If possible decrease the size of the bar code to help make room for required labeling statements.

Due to the complicated nature of revisions, we have included a crude draft of the revisions. We have used the Adult 22.5 mg for 3 month administration NDA 020517 as the beginning template to show the revisions because this version incorporated the previous recommendations from the Agency. This draft should be used only to guide the placement of information and not the content. Although we are providing this draft layout, alternate proposals can be made, provided they include all of the same information.

### **Lupaneta Outer Carton Labeling**

1. Revise the presentation of the proposed proprietary name to “Lupaneta Pack” and present the entire proposed proprietary name as title case (i.e., Lupaneta Pack) and in a single color font size, and type. The use of all capital letters for the word “PACK” and the use of two different colors is a form of tall man lettering. We reserve tall man lettering for established names with known name confusion. Additionally, presenting the name in one color, font size, and font type will help reinforce the entire proprietary name as “Lupaneta Pack.”
2. Revise the established name to have a prominence commensurate with the prominence of the proprietary name, including typography, layout, contrast, and other printing features per 21 CFR 201.10(g)(2).

Revise the established name presentation to include the strength of each component of Lupaneta Pack following the dosage form statement. Additionally, ensure the strength of the Leuprolide Acetate component (i.e., 3.75 mg and 11.25 mg) is prominent (i.e., using a larger font size). Incorporating the strength statement can provide another tool (in addition to the frequency of administration: ‘1-month’ and ‘3-month’) to help differentiate the two different Lupaneta Pack products and may help mitigate the risk of medication errors due to product selection. The revised presentation may appear as follows:

#### **Lupaneta Pack**

leuprolide acetate for depot suspension,  
3.75 mg for intramuscular injection only  
and Norethindrone Acetate Tablets, 5 mg for oral administration

#### **Lupaneta Pack**

leuprolide acetate for depot suspension,  
11.25 mg for intramuscular injection only  
and Norethindrone Acetate Tablets, 5 mg for oral administration

3. Replace the ‘plus sign’ within the established name with the word ‘and.’

4. Remove the large plus sign that appears on the left hand side of the proprietary and the established names, as well as the lower right hand side of all the side panels where it appears. As currently presented, the large plus sign can distract from the proprietary name and the frequency of administration.
5. Remove the two-toned color band that contains the proprietary and the established names, as well as the frequency of administration. The color band should be used only for the frequency of administration, consistent with DMEPA's recommendations for the Lupron Depot products.
6. Increase the prominence of the frequency of administration statement on the top right hand side of the display panel by increasing the font size, bolding, and using dark ink against a light purple color block, to increase contrast. It is important to provide visual differentiation between the 1-month and the 3-month frequency of administrations of Lupaneta Pack to minimize medication errors due to selection errors in the pharmacy.
7. Include the Usual Dose for Norethindrone Acetate on the principal display panel. As currently presented, this information does not appear under the second bullet point. The statement may appear as:

'Usual Dose: Take 5 mg (one tablet) orally once daily for 1 month (or 3 months). See package insert for full prescribing information.'
8. Reduce the prominence of the company name and logo on the principal display panel. As currently presented, this information competes in prominence with the proprietary name and the frequency of administration statement.
9. Expiration date and Lot number for the co-packaged product should be displayed on the carton label. The expiration date should be the same as the product whichever expires earlier.
10. Storage condition should be displayed for the co-packaged product in addition to the storage condition of individual product. The storage condition for the co-packaged product should be displayed as "Store at 25°C (77°F), excursion permitted to 15°C- 30°C (59-86°F) [See USP Controlled Room Temperature]."
11. (b) (4) "Not made with natural rubber latex."

If you have any questions, call Kim Shiley, R.N., B.S.N., Regulatory Project Manager, at (301) 796-2117.

Sincerely,

*{See appended electronic signature page}*

Audrey Gassman, M.D.

Acting Deputy Director

Division of Reproductive and Urologic Products

Office of Drug Evaluation III

Center of 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/  
-----

AUDREY L GASSMAN  
11/02/2012

**Shiley, Kimberly**

**From:** Greeley, George  
**Sent:** Monday, June 11, 2012 11:01 AM  
**To:** Mercier, Jennifer L  
**Cc:** Suggs, Courtney; Kober, Margaret; Shiley, Kimberly  
**Subject:** RE: Possible submissions that may require PeRC review

Hi Jennifer,

Thank you for responding to Courtney's inquiry for the list of products. It's interesting that you would ask the question about NDA 203-696 as I had just completed a call with Kim regarding this product. This product would not trigger PREA based on co-packaging alone. For those NDAs that do not trigger PREA we ask that the pediatric page be completed down to question 2b.

Thanks,  
George

---

**From:** Mercier, Jennifer L  
**Sent:** Monday, June 11, 2012 10:27 AM  
**To:** Suggs, Courtney; Kober, Margaret  
**Cc:** Greeley, George  
**Subject:** RE: Possible submissions that may require PeRC review

NDA 204061 - yes  
NDA 203696 - the sponsor is co-packaging existing products, so not sure - please advise  
(b) (4) - yes  
NDA 203505 - yes  
NDA 21998 - this is with DNDC (OTC) it is to lower the age for OTC use.

---

**From:** Suggs, Courtney  
**Sent:** Wednesday, June 06, 2012 12:53 PM  
**To:** Kober, Margaret; Mercier, Jennifer L  
**Cc:** Greeley, George  
**Subject:** Possible submissions that may require PeRC review

Dear Margaret and Jennifer,

The following submissions have a PDUFA goal date in the near future. Please help us by letting us know if these applications trigger PREA or are in response to a PREA post-marketing commitment/requirement.

204061	NDA	1	Dr-103	DRUP
203696	NDA	1	Leuprolide Acetate For Depot Suspension And Norethindrone Acetate Tablets	DRUP
(b) (4)				
203505	NDA	1	Ospemifene Tablets	DRUP
21998	PAT POPUL	2	Plan B One-step	DRUP

As a reminder, PREA triggers include the following

- New active ingredient
- New dosage form

- New route of administration
- New indication
- New dosing regimen

If PREA is triggered for any of these submissions or if they are in response to a PREA postmarketing commitment/requirement, contact Courtney Suggs or George Greeley to schedule a time for PeRC to review. Please let me know if your division plans to act early on this application so we can plan a PeRC date prior to approval.

Thanks,  
Courtney

## Courtney M. Suggs, Pharm.D., MPH

LCDR, USPHS  
Regulatory Project Manager  
Pediatric and Maternal Health Staff  
Office of New Drugs, Immediate Office  
Center for Drug Evaluation and Research  
US Food and Drug Administration  
10903 New Hampshire Ave.  
Bldg 22, Room 6471  
Silver Spring, MD 20993  
Phone: (301) 796-2096  
Email: [courtney.suggs@fda.hhs.gov](mailto:courtney.suggs@fda.hhs.gov)



NDA 203696

**PROPRIETARY NAME REQUEST  
WITHDRAWN**

Abbott Endocrine Inc.  
200 Abbott Park Road  
Dept PA 77/Bldg. AP34-3  
Abbott Park, IL 60064-6157

ATTENTION: Leslie Bennett, RAC (US EU),  
Director, Regulatory Affairs-PPG

Dear Ms. Bennett:

Please refer to your New Drug Application (NDA) dated February 15, 2012, received February 15, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Leuprolide Acetate For Depot Suspension and Norethindrone Acetate Tablets Co-packaged kits, 3.75 mg/5 mg and 11.25 mg/5 mg.

We acknowledge receipt of your correspondence, dated and received May 22, 2012, notifying us that you are withdrawing your April 10, 2012 request for a review of the proposed proprietary name [REDACTED] (b)(4). This proposed proprietary name request is considered withdrawn as of May 22, 2012.

We note that you have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, a new request for a proposed proprietary name review should be submitted.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Maria Wasilik, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0567. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Kim Shiley at (301)796-2117.

Sincerely,

*{See appended electronic signature page}*

Carol Holquist, RPh  
Director  
Division of Medication Error Prevention and Analysis  
Office of Medication Error Prevention and Risk Management  
Office of Surveillance and Epidemiology  
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/  
-----

CAROL A HOLQUIST  
06/06/2012

**MEMORANDUM**

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

**MEETING DATE:** 4-16-2012  
**TIME:** 12:00 pm  
**LOCATION:** WO 22 Room 4311  
**APPLICATION:** NDA 203696

**DRUG NAME:** (b) (4) (leuprolide acetate for depot suspension and norethindrone acetate tablets)

**TYPE OF MEETING:** Teleconference

**APPLICANT:** Abbott Endocrine Inc.

**FDA ATTENDEES:** Maria Wasilik, OSE Safety Project Manager  
Zach Oleszczuk, DMEPA Team Leader  
Manizheh Siahpoushan, DMEPA Safety Evaluator  
Kim Shiley, DRUP Regulatory Project Manager  
Margie Kober, DRUP Chief Project Management Staff

**EXTERNAL CONSTITUENT ATTENDEES:**

Leslie Bennett, Director Regulatory Affairs (US/Can)  
Alison Boswell, Director Commercial Strategy  
Amol Luktuke, Manager Product  
Peter Bacher, Project Director  
Faraneh Attarchi, Director Global Regulatory

**Background:**

DMEPA requested this teleconference to inform the Applicant of concerns with the proposed proprietary name, (b) (4)

**Discussion:**

During the preliminary assessment of the proposed name, (b) (4) DMEPA had a concern with the name (b) (4)

(b) (4)

DMEPA recommends against using tall man lettering because this naming strategy is reserved as a tool to differentiate established names that are orthographically similar. They also recommend against using any abbreviations or modifiers. A single name incorporating part of both ingredient names would be acceptable for this product as long as it is not orthographically or phonetically similar to Lupron.

**Regulatory Steps Forward:**

1. FDA can finalize the proprietary name review for [REDACTED] (b) (4) and issue a denial letter regarding your proposed name which would be issued on or before the OSE PDUFA date of 7/9/12.
2. Withdraw the proprietary name request for [REDACTED] (b) (4) and submit an alternate name for review.

**Questions/Comments:**

**Conclusion:**

The Applicant will withdraw the name and submit alternative names for review within a week.

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

/s/  
-----

MARIA R WASILIK  
05/04/2012



NDA 203696

## FILING COMMUNICATION

Abbott Endocrine Inc.  
Attention: Leslie Bennett  
Director, RA-Area and Affiliate Strategy  
200 Abbott Park Road  
Dept PA77/Bldg. AP34  
Abbott Park, IL 60064-6157

Dear Ms. Bennett:

Please refer to your New Drug Application (NDA) dated and received February 15, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for leuprolide acetate for depot suspension and norethindrone acetate tablets co-packaged kits.

We also refer to your amendment dated March 30, 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 15, 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, midcycle, 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 November 17, 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 a 4-month safety update that includes a review of the current literature and a summary of postmarketing information. The Periodic Safety Update Report may

be sufficient to address postmarketing safety if the cut-date for the information in the report is close to the cut-date for the 4-month safety update.

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

### **Full Prescribing Information (FPI)**

- **Adverse Reactions**

- Only “adverse reactions” as defined in 21 CFR 201.57(c)(7) should be included in labeling. Other terms, such as “adverse events” or “treatment-emergent adverse events,” should be avoided.
- For the “Clinical Trials Experience” subsection, the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

“Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.”
- For the “Postmarketing Experience” subsection, the listing of post-approval adverse reactions must be separate from the listing of adverse reactions identified in clinical trials. Include the following verbatim statement or appropriate modification:

“The following adverse reactions have been identified during post-approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.”

- **Patient Counseling Information**

- Must reference any FDA-approved patient labeling, including the type of patient labeling. The statement “See FDA-approved patient labeling (insert type of patient labeling).” should appear at the beginning of Section 17 for prominence. For example:
  - “See FDA-approved patient labeling (Patient Information)”

We request that you resubmit labeling that addresses these issues by May 18, 2012. The resubmitted labeling will be used for further labeling discussions.

### **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) and patient PI. 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 patient PI, 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 acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Kim Shiley, R.N., B.S.N., Regulatory Health Project Manager, at (301) 796-2117.

Sincerely,

*{See appended electronic signature page}*

Audrey Gassman, M.D.  
Acting Deputy Director  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
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/  
-----

AUDREY L GASSMAN  
04/26/2012



NDA 203696

**NDA ACKNOWLEDGMENT**

Abbott Endocrine Inc.  
Attention: Leslie Bennett  
Director, RA-Area and Affiliate Strategy  
200 Abbott Park Road  
Dept PA77/Bldg. AP34  
Abbott Park, IL 60064-6157

Dear Ms. Bennett:

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

Name of Drug Product: Leuprolide acetate for depot suspension and norethindrone acetate tablets co-packaged kits

Date of Application: February 15, 2012

Date of Receipt: February 15, 2012

Our Reference Number: NDA 203696

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 15, 2012, in accordance with 21 CFR 314.101(a).

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 Reproductive and Urologic Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

If you have any questions, call Kim Shiley, R.N., B.S.N., Regulatory Health Project Manager, at (301) 796-2117.

Sincerely,

*{See appended electronic signature page}*

Margaret Kober, R.Ph., M.P.A.  
Chief, Project Management Staff  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
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/  
-----

MARGARET M KOBER  
04/05/2012  
Chief, Project Management Staff



(b) (4)

**MEETING MINUTES**

Abbott Endocrine, Inc.  
Attention: Jean Conaway, R.Ph., R.A.C., M.B.A.  
Associate Director, Regulatory Affairs - PPG  
200 Abbott Park Road  
D-PA77/AP30-1NE  
Abbott Park, IL 60064

Dear Ms. Conaway:

Please refer to your Pre-Investigational New Drug Application (PIND) file for your proposed co-packaged product containing Lupron Depot<sup>®</sup> (leuprolide acetate for depot suspension) and norethindrone acetate tablets.

We also refer to the teleconference between representatives of your firm and the FDA on November 10, 2011. The purpose of the meeting was to obtain FDA guidance on the content and format of your NDA submission for a proposed leuprolide acetate depot injection (Lupron Depot) and norethindrone acetate tablets co-packaged kit.

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

If you have any questions, call Kim Shiley, R.N., B.S.N., Regulatory Health Project Manager at (301) 796-2117.

Sincerely,

*{See appended electronic signature page}*

Lisa Soule, M.D.  
Clinical Team Leader  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

ENCLOSURE:  
Meeting Minutes

## MEMORANDUM OF MEETING MINUTES

**Meeting Type:** Type B  
**Meeting Category:** Pre-NDA

**Meeting Date and Time:** November 10, 2011, 11:00 AM – 12:00 PM  
**Meeting Location:** Teleconference

**Application Number:** 110735  
**Product Name:** co-packaged product containing Lupron Depot<sup>®</sup>  
(leuprolide acetate for depot suspension) and  
norethindrone acetate tablets.

**Indication:** endometriosis  
**Sponsor/Applicant Name:** Abbott Endocrine, Inc.

**Meeting Chair:** Lisa Soule, M.D.  
**Meeting Recorder:** Kim Shiley, R.N.

### FDA ATTENDEES

#### Division of Reproduction and Urologic Products

Lisa Soule, M.D., Clinical Team Leader  
Ronald Orleans, M.D., Medical Officer  
Margaret Kober, R.Ph., M.P.A., Chief, Project Management Staff  
Kim Shiley, R.N., B.S.N., Regulatory Health Project Manager

#### Division of Clinical Pharmacology III

Li Li, Ph.D., Clinical Pharmacology Reviewer  
Sayed (Sam) Al Habet, R.Ph., Ph.D., Clinical Pharmacology Acting Team Leader

#### Office of New Drug Quality Assessment

Donna Christner, Ph.D., CMC Lead

#### Office of Generic Drugs, Division of Chemistry IV

Upinder S. Atwal, Ph.D., Chemistry Team Leader

### SPONSOR ATTENDEES

H. Peter Bacher, M.D., Ph.D., Project Director, Global Pharmaceutical Research and Development  
Jean Conaway, R.Ph., R.A.C., M.B.A., Regulatory Affairs, Pharmaceutical Products Group  
Dean Coombes, Associate Director, C.M.C., Regulatory Affairs  
B. Robert Imani, M.D., Ph.D., Senior Medical Director, Postmarketing Safety Evaluation, Global Pharmacovigilance, Global Medical Service

Ping Jiang, Associate Director, Statistics  
Udo Legler, M.D., Ph.D., Diplomat, Biochemistry Director and Head  
Aline Lindbeck, Ph.D., Assistant Director, Drug Development, Project Management  
Lisa Marshall, PharmD., Manager, Small Molecule, CMC Reg Affairs  
Alan McEmber, M.S., R.A.C., Sr. Director, Therapeutic Head, Regulatory Affairs  
Bruce Yamamoto R.D., M.B.A., Periodic Reports Manager

## **BACKGROUND**

On March 23, 2011, the Division provided written advice as requested by the Sponsor regarding the Sponsor's proposed co-packaged product, leuprolide acetate depot injection (Lupron Depot) and norethindrone acetate tablets. On September 6, 2011, the Sponsor requested a meeting to obtain guidance on the content and format of their NDA submission for this proposed co-packaged kit. The Division provided Preliminary Meeting Comments to the Sponsor on November 8, 2011.

## **DISCUSSION**

### **Clinical/Statistics/Nonclinical**

*1. Does the Agency agree to consider the proposed indication for the Lupron Co-Pack presentation?*

#### **Division Response:**

While the Division will consider the proposed indication, it is concerned about a potential broadening of the indication beyond what was previously proposed by the Division.

#### **Additional Discussion at the Meeting:**

The Sponsor requested clarification regarding the Division's concern regarding "potential broadening" of the indication. The Sponsor stated that it did not intend for its proposed revised indication to broaden the indication beyond what was previously proposed by the Division. The Sponsor agreed to use the Division's March 23, 2011 suggested wording for the indication as follows:

TRADENAME is indicated for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms. Duration of initial treatment or retreatment should be limited to 6 months.

*2. Does the Agency agree that it is acceptable to cross-reference the historical Lupron NDAs that supported the approval of the Lupron add-back indication and that no documents need to be included in Module 2, 4, and 5 (with the exception that the PSUR will be included in Module 5) for the proposed Lupron Co-Pack NDA?*

#### **Division Response:**

Yes.

3. *Abbott proposes that the most recent PSUR will be provided in the proposed NDA (in Module 5.3.6) and no other safety information (including a 4-month safety update) will be required. Does the Agency agree?*

**Division Response:**

No; the Sponsor should also provide a 120-day safety update.

**Additional Discussion at the Meeting:**

The Sponsor noted there are “no ongoing studies” and requested clarification regarding what is required. The Division reiterated that the 120-day safety update is a standard feature of an NDA submission, which should include reviews of the current literature and a summary of postmarketing safety information. The Periodic Safety Update Report (PSUR) might be sufficient to address the postmarketing safety information provided the cut-date for the information in that report is reasonably close to the cut-date for the 120-day safety update.

**CMC**

4. *Does the Agency agree that it is acceptable to cross-reference the historical CMC information from the original applications to support the proposed Lupron Co-Pack NDA submission?*

**Division Response:**

It is acceptable to cross-reference the majority of the information from the previously approved applications. However, the following information should be submitted to the new NDA:

- In the NDA submission, provide a comprehensive table/list of all facilities involved in production of the drug substance(s) and drug product(s) with full street address of the actual manufacturing and/or testing site (not the corporate office), contact information of an individual at the site, detailed responsibilities of that facility and a date of when the facility was last inspected by FDA. This information will help to facilitate inspection requests. This comprehensive table should be attached to the 356h. Full information should still be provided in the appropriate sections of Module 3. See additional comments in response to Question 8 for more information on the 356h attachment.
- In addition to the planned submission of Letters of Authorization (LOAs) for the cross-referenced approved applications, include LOAs for any supporting submissions (i.e., DMFs) to this NDA.
- Submit specific cross-references (amendment numbers and submission dates) to the most current information in the approved applications.

For ease of review, the Division requests that the following information also be provided in this NDA:

- Drug Substance(s)
  - General information
  - Physico-chemical properties
  - Specifications
- Drug Products(s)
  - Formulation

- Specifications
- Brief description and/or flow chart of the manufacturing process
- Overview of stability data generated to date

**Additional Discussion at the Meeting:**

The Sponsor requested clarification about providing a LOA to allow the Division to review cross-referenced information, citing a concern that some of the requested information is proprietary and might not be shared directly with the Sponsor. The Division will clarify in a post meeting comment.

**Post-meeting Comment:**

LOAs should be provided to the new NDA so that the Division can access the proprietary information in support of this NDA. This will provide up-to-date information on manufacturing facilities so that the appropriate inspections can be requested. This will also require the DMF holders to report any future changes to the new NDA and the cross-referenced ANDA so that appropriate steps can be taken by all applicants.

**Regulatory**

*5. Does the Agency agree with the proposal to provide one combined physician package insert that contains two separate portions (Lupron/NETA) for inclusion in the proposed Lupron Co-Pack Kit?*

**Division Response:**

No. The Sponsor should submit integrated labeling in Physician Labeling Rule (PLR) format that includes those portions of NETA labeling pertinent to this product. The Division also recommends that the Sponsor consider recent PLR labeling for an oral contraceptive product (such as Lo Loestrin Fe) for guidance in preparing the labeling regarding the NETA component.

For guidance on preparing an integrated label that covers two drug products, labeling for the following co-packaged product may be useful:

- Omeprazole, clarithromycin, and amoxicillin for H. pylori

In addition, the Division has the following general comments:

- Proposed prescribing information (PI) submitted with the application must conform to the content and format regulations found at 21 CFR 201.56 and 201.57.
- Summary of the Final Rule on the Requirements for Prescribing Information for Drug and Biological Products, labeling guidances, sample tool illustrating Highlights and Table of Contents, an educational module concerning prescription drug labeling, and fictitious prototypes of prescribing information are available at: <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActs/andRules/ucm084159.htm>. The Division encourages the Sponsor to review the information at this website and use it as it drafts prescribing information for its application.

6. *Abbott proposes that the Lupron Co-Pack NDA will be submitted approximately 30 days after Glenmark submits the CBE-30 to OGD for NETA 30 tablet and 90 tablet/bottle package configurations. Since the Lupron Co-Pack NDA will cross-reference the Glenmark ANDA for the NETA component, does the Agency agree that the review of the NDA for the Lupron Co-Pack kit can occur concurrently at the time as the OGD review of the NETA CBE-30 and that it is not necessary to obtain OGD written approval of the CBE-30 prior to initiating review of the Lupron Co-Pack NDA?*

**Division Response:**

Yes. The timing for submission of the supplement to the Office of Generic Drugs (OGD) in relation to the timing for submission of the NDA for the co-packaged product is reasonable. The Division agrees that the review times can overlap. Note, however, that OGD must approve the supplement before the Division can approve the NDA.

**Additional Discussion at the Meeting:**

The Sponsor inquired as to how the Division will be notified of Glenmark's ANDA supplement approval with the Office of Generic Drugs (OGD). OGD stated that they will inform the Division of approval or non-approval. The Sponsor plans to submit its NDA at the end of December or early January 2012. The Sponsor believes that Glenmark will be submitting the ANDA soon (30 days prior to the planned submission of the NDA).

7. *Does the Agency agree that the proposed waivers may be considered for the planned NDA submission?*

**Division Response:**

The Sponsor should provide data supporting the rarity of endometriosis in women under age 18 in order to support a full waiver request in pediatric females. Alternatively, the Sponsor could request a partial waiver of studies in premenarcheal females and extrapolation of data from adult women to address the need for data in postmenarcheal pediatric patients. The Pediatric Research Committee will be consulted regarding this matter.

8. *Does the Agency have any additional comments on the proposed Lupron Co-Pack NDA submission?*

**Division Response:**

To facilitate the inspectional process, the Office of Manufacturing and Product Quality in CDER's Office of Compliance requests that the Sponsor clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided

in the attachment titled, "Product name, NDA/BLA 012345, Establishment Information for Form 356h."

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
1.				
2.				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
1.				
2.				

**ISSUES REQUIRING FURTHER DISCUSSION**

There were no issues requiring further discussion

**ACTION ITEMS**

Action Item/Description	Owner	Due Date
Provide meeting minutes	FDA	30 days

**ATTACHMENTS AND HANDOUTS**

There were no attachments or handouts for the meeting minutes.

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

/s/  
-----

LISA M SOULE  
12/09/2011