

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**204734Orig1s000**

**ADMINISTRATIVE and CORRESPONDENCE**  
**DOCUMENTS**

Department of Health and Human Services  
Food and Drug Administration

Form Approved: OMB No. 0910-0513  
Expiration Date: 10/31/2013  
See OMB Statement on Page 3.

**PATENT INFORMATION SUBMITTED WITH THE FILING  
OF AN NDA, AMENDMENT, OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance  
(Active Ingredient), Drug Product (Formulation and Composition)  
and/or Method of Use*

NDA NUMBER

204734

NAME OF APPLICANT/NDA HOLDER

Shire Development LLC

*The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.*

TRADE NAME (OR PROPOSED TRADE NAME)

FOSRENOL® Oral Powder

ACTIVE INGREDIENT(S)

lanthanum carbonate

STRENGTH(S)

750mg and 1000mg

DOSAGE FORM

Oral powder

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the *only* information relied upon by FDA for listing a patent in the Orange Book.

**For hand-written or typewriter versions (only) of this report:** If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

**FDA will not list patent information if you submit an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.**

**For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.**

**1. GENERAL**

a. United States Patent Number

5,968,976

b. Issue Date of Patent

October 19, 1999

c. Expiration Date of Patent

October 26, 2018

d. Name of Patent Owner

Shire International Licensing B.V.

Address (of Patent Owner)

Strawinsyiaan 847

City/State

Amsterdam

ZIP Code

1077 XX Netherlands

FAX Number (if available)

Telephone Number

+33 20 470 8425

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.62 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Shire Development LLC

Address (of agent or representative named in 1.e.)

725 Chesterbrook Blvd.

City/State

Wayne, PA

ZIP Code

19087

FAX Number (if available)

484-595-8156

Telephone Number

484-595-5368

E-Mail Address (if available)

sgirty@shire.com

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

**2. Drug Substance (Active Ingredient)**

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?  Yes  No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?  Yes  No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).  Yes  No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)  Yes  No

2.6 Does the patent claim only an intermediate?  Yes  No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)  Yes  No

**3. Drug Product (Composition/Formulation)**

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?  Yes  No

3.2 Does the patent claim only an intermediate?  Yes  No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)  Yes  No

**4. Method of Use**

Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) 7 - 10 Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the proposed labeling.)  
The proposed labeling indication for FOSRENOL® Oral Powder is to reduce serum phosphate in patients with end stage renal disease (ESRD).

**5. No Relevant Patents**

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.  Yes

**6. Declaration Certification**

6.1 *The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.*

*Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.*

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed



27 Feb 2013

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Sabrina Girty, J.D.

Address

Shire Development LLC  
725 Chesterbrook Blvd.

City/State

Wayne, PA

ZIP Code

19087

Telephone Number

484-595-5368

FAX Number (if available)

484-595-8156

E-Mail Address (if available)

sgirty@shire.com

The public reporting burden for this collection of information has been estimated to average 20 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services  
Food and Drug Administration  
Office of Chief Information Officer  
1350 Piccard Drive, Room 400  
Rockville, MD 20850

*An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.*

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**1. GENERAL**

a. United States Patent Number

7,465,465

b. Issue Date of Patent

December 16, 2008

c. Expiration Date of Patent

August 26, 2024

d. Name of Patent Owner

Shire International Licensing B.V.

Address (of Patent Owner)

Strawinsyiaan 847

City/State

Amsterdam

ZIP Code

1077 XX Netherlands

FAX Number (if available)

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Shire Development LLC

Address (of agent or representative named in 1.e.)

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City/State

Wayne, PA

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Yes

No

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No

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2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).  Yes  No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

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**3. Drug Product (Composition/Formulation)**

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?  Yes  No

3.2 Does the patent claim only an intermediate?  Yes  No

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**4. Method of Use**

**Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the proposed labeling.)

**5. No Relevant Patents**

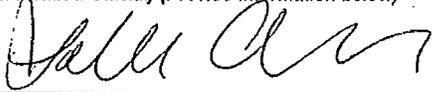
For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.  Yes

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Date Signed

27 Feb 2013

**NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).**

Check applicable box and provide information below.

|  |   |
|--|---|
| <input checked="" type="checkbox"/> NDA Applicant/Holder   | <input type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official |
| <input type="checkbox"/> Patent Owner                      | <input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official           |
| Name<br>Sabrina Girty, J.D.                                |   |
| Address<br>Shire Development LLC<br>725 Chesterbrook Blvd. | City/State<br>Wayne, PA   |
| ZIP Code<br>19087  | Telephone Number<br>484-595-5368  |
| FAX Number (if available)<br>484-595-8156                  | E-Mail Address (if available)<br>sgirty@shire.com   |

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Department of Health and Human Services  
Food and Drug Administration  
Office of Chief Information Officer  
1350 Piccard Drive, Room 400  
Rockville, MD 20850

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## EXCLUSIVITY SUMMARY

NDA # 204734

SUPPL #

HFD #

Trade Name Fosrenol

Generic Name lanthanum carbonate

Applicant Name Shire Development LLC

Approval Date, If Known

### 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.

A single pharmacokinetic/pharmacodynamic study conducted in healthy subjects was submitted to demonstrate pharmacodynamic equivalence between the two dosage forms and establish a bridge between Fosrenol oral powder and Fosrenol chewable tablet.

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# 021468                      lanthanum carbonate

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

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

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

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



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

/s/  
-----

MICHAEL V MONTELEONE  
09/24/2014

NORMAN L STOCKBRIDGE  
09/24/2014

### 1.3.3 DEBARMENT CERTIFICATION

Shire Development LLC (Shire) 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.



Sabrina Girty, J.D.  
Director, Global Regulatory Affairs

# ACTION PACKAGE CHECKLIST

| APPLICATION INFORMATION <sup>1</sup>   |  |  |
|--|--|--|
| NDA # 204734<br>BLA #  | NDA Supplement #<br>BLA Supplement #   | If NDA, Efficacy Supplement Type:<br><i>(an action package is not required for SE8 or SE9 supplements)</i> |
| Proprietary Name: Fosrenol<br>Established/Proper Name: lanthanum carbonate<br>Dosage Form: oral powder   |  | Applicant: Shire Development, LLC<br>Agent for Applicant (if applicable):                                  |
| RPM: Michael Monteleone  |  | Division: Cardiovascular and Renal Drug Products   |
| NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)<br>Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)<br><br>BLA Application Type: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a)<br>Efficacy Supplement: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a)  | <p><b><u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u></b></p> <ul style="list-style-type: none"> <li>Review the information in the 505(b)(2) Assessment and submit the draft<sup>2</sup> to CDER OND IO for clearance.</li> <li>Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)</li> </ul> <p><input type="checkbox"/> No changes<br/> <input type="checkbox"/> New patent/exclusivity (<i>notify CDER OND IO</i>)<br/>           Date of check:</p> <p><i>Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</i></p> |  |
| ❖ Actions  |  |  |
| <ul style="list-style-type: none"> <li>Proposed action</li> <li>User Fee Goal Date is <u>September 30, 2014</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 type="checkbox"/> None CR – 2013-12-24  |
| ❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received?<br>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 _____ |  | <input type="checkbox"/> Received  |
| ❖ Application Characteristics <sup>3</sup>   |  |  |

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

<sup>2</sup> For resubmissions, 505(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).

<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.

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

- |   |   |
|---|---|
| <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            |
| <input type="checkbox"/> Breakthrough Therapy designation |   |

NDAs: Subpart H

- Accelerated approval (21 CFR 314.510)  
 Restricted distribution (21 CFR 314.520)

Subpart I

- Approval based on animal studies

- Submitted in response to a PMR  
 Submitted in response to a PMC  
 Submitted in response to a Pediatric Written Request

BLAs: Subpart E

- Accelerated approval (21 CFR 601.41)  
 Restricted distribution (21 CFR 601.42)

Subpart H

- Approval based on animal studies

- REMS:  MedGuide  
 Communication Plan  
 ETASU  
 MedGuide w/o REMS  
 REMS not required

Comments:

|   |   |
|---|---|
| ❖ 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  |
| ❖ Public communications ( <i>approvals only</i> )   |   |
| • Office of Executive Programs (OEP) liaison has been notified of action  | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |
| • Indicate what types (if any) of information were issued   | <input checked="" type="checkbox"/> None<br><input type="checkbox"/> FDA Press Release<br><input type="checkbox"/> FDA Talk Paper<br><input type="checkbox"/> CDER Q&As<br><input type="checkbox"/> Other |
| ❖ Exclusivity   |   |
| • Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)?<br>• If so, specify the type          | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes   |
| ❖ Patent Information (NDAs only)  |   |
| • Patent Information:<br>Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.                                 | <input checked="" type="checkbox"/> Verified<br><input type="checkbox"/> Not applicable because drug is an old antibiotic.  |
| <b>CONTENTS OF ACTION PACKAGE</b>   |   |
| <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  |

| Action Letters   |   |
|--|---|
| ❖ Copies of all action letters <i>(including approval letter with final labeling)</i>  | Action(s) and date(s)<br>AP 9-24-2014<br>CR 12-24-2013  |
| Labeling   |   |
| ❖ 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 <i>(if it is division-proposed labeling, it should be in track-changes format)</i></li> </ul>  | <input checked="" type="checkbox"/> Included  |
| <ul style="list-style-type: none"> <li>Original applicant-proposed labeling</li> </ul>   | <input checked="" type="checkbox"/> Included  |
| ❖ 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<br><input type="checkbox"/> Patient Package Insert<br><input type="checkbox"/> Instructions for Use<br><input type="checkbox"/> Device Labeling<br><input type="checkbox"/> None   |
| <ul style="list-style-type: none"> <li>Most-recent draft labeling <i>(if it is division-proposed labeling, it should be in track-changes format)</i></li> </ul>  | <input type="checkbox"/> Included   |
| <ul style="list-style-type: none"> <li>Original applicant-proposed labeling</li> </ul>   | <input checked="" type="checkbox"/> Included  |
| ❖ 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>   |   |
| <ul style="list-style-type: none"> <li>Most-recent draft labeling</li> </ul>   | <input checked="" type="checkbox"/> Included  |
| ❖ Proprietary Name   | N/A   |
| <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> </ul>   |   |
| ❖ Labeling reviews <i>(indicate dates of reviews)</i>  | RPM: <input type="checkbox"/> None<br>DMEPA: <input type="checkbox"/> None 2014-08-29;<br>2013-10-07<br>DMPP/PLT (DRISK):<br><input type="checkbox"/> None<br>OPDP: <input type="checkbox"/> None 2013-11-27<br>SEALD: <input type="checkbox"/> None 2013-12-20<br>CSS: <input type="checkbox"/> None<br>Other: <input type="checkbox"/> None |
| Administrative / Regulatory Documents  |   |
| ❖ RPM Filing Review <sup>4</sup> /Memo of Filing Meeting <i>(indicate date of each review)</i>   | 2013-04-29  |
| ❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee   | <input checked="" type="checkbox"/> Not a (b)(2)  |
| ❖ NDAs only: Exclusivity Summary <i>(signed by Division Director)</i>  | <input checked="" type="checkbox"/> Included  |
| ❖ Application Integrity Policy (AIP) Status and Related Documents<br><a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a> |   |
| <ul style="list-style-type: none"> <li>Applicant is on the AIP</li> </ul>  | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |

<sup>4</sup> Filing reviews for scientific disciplines are NOT required to be included in the action package.

|  |  |
|--|--|
| <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 type="checkbox"/> No<br><br><input type="checkbox"/> Not an AP action  |
| ❖ Pediatrics ( <i>approvals only</i> ) <ul style="list-style-type: none"> <li>• Date reviewed by PeRC <u>2013-10-09</u><br/>If PeRC review not necessary, explain: _____</li> </ul>  |  |
| ❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, etc.) ( <i>do not include previous action letters, as these are located elsewhere in package</i> )   | Included   |
| ❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)  |  |
| ❖ Minutes of Meetings <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> <li>• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)</li> <li>• EOP2 meeting (<i>indicate date of mtg</i>)</li> <li>• Mid-cycle Communication (<i>indicate date of mtg</i>)</li> <li>• Late-cycle Meeting (<i>indicate date of mtg</i>)</li> <li>• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)</li> </ul> | <input type="checkbox"/> N/A or no mtg    2014-05-14<br><input type="checkbox"/> No mtg<br><input type="checkbox"/> No mtg<br><input type="checkbox"/> N/A<br><input type="checkbox"/> N/A |
| ❖ Advisory Committee Meeting(s) <ul style="list-style-type: none"> <li>• Date(s) of Meeting(s)</li> </ul>  | <input checked="" type="checkbox"/> No AC meeting  |
| <b>Decisional and Summary Memos</b>  |  |
| ❖ Office Director Decisional Memo ( <i>indicate date for each review</i> )   | <input type="checkbox"/> None  |
| Division Director Summary Review ( <i>indicate date for each review</i> )  | <input type="checkbox"/> None    2014-09-24;<br>2013-12-24   |
| Cross-Discipline Team Leader Review ( <i>indicate date for each review</i> )   | <input type="checkbox"/> None    2013-12-21  |
| PMR/PMC Development Templates ( <i>indicate total number</i> )   | <input type="checkbox"/> None    2014-09-09  |
| <b>Clinical</b>  |  |
| ❖ Clinical Reviews <ul style="list-style-type: none"> <li>• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)</li> <li>• Clinical review(s) (<i>indicate date for each review</i>)</li> <li>• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)</li> </ul>   | <input checked="" type="checkbox"/> No separate review<br>2013-10-28; 2013-04-10<br><input type="checkbox"/> None  |
| ❖ Financial Disclosure reviews(s) or location/date if addressed in another review<br>OR<br>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> )   |  |
| ❖ 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"/> N/A  |

|   |   |
|---|---|
| ❖ Risk Management <ul style="list-style-type: none"> <li>REMS Documents and REMS Supporting Document (<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 type="checkbox"/> None                                 |
| ❖ OSI Clinical Inspection Review Summary(ies) ( <i>include copies of OSI letters to investigators</i> )   | <input checked="" type="checkbox"/> None requested            |
| <b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None   |   |
| ❖ Clinical Microbiology Team Leader Review(s) ( <i>indicate date for each review</i> )  | <input type="checkbox"/> No separate review                   |
| Clinical Microbiology Review(s) ( <i>indicate date for each review</i> )  | <input type="checkbox"/> None                                 |
| <b>Biostatistics</b> <input type="checkbox"/> None  |   |
| ❖ Statistical Division Director Review(s) ( <i>indicate date for each review</i> )  | <input checked="" type="checkbox"/> No separate review        |
| Statistical Team Leader Review(s) ( <i>indicate date for each review</i> )  | <input checked="" type="checkbox"/> No separate review        |
| Statistical Review(s) ( <i>indicate date for each review</i> )  | <input type="checkbox"/> None 2013-04-18                      |
| <b>Clinical Pharmacology</b> <input type="checkbox"/> None  |   |
| ❖ Clinical Pharmacology Division Director Review(s) ( <i>indicate date for each review</i> )  | <input checked="" type="checkbox"/> No separate review        |
| Clinical Pharmacology Team Leader Review(s) ( <i>indicate date for each review</i> )  | <input checked="" type="checkbox"/> No separate review        |
| Clinical Pharmacology review(s) ( <i>indicate date for each review</i> )  | <input type="checkbox"/> None 2013-10-28;2013-04-18           |
| ❖ OSI Clinical Pharmacology Inspection Review Summary ( <i>include copies of OSI letters</i> )  | <input type="checkbox"/> None requested                       |
| <b>Nonclinical</b> <input type="checkbox"/> None  |   |
| ❖ Pharmacology/Toxicology Discipline Reviews  |   |
| • ADP/T Review(s) ( <i>indicate date for each review</i> )  | <input type="checkbox"/> No separate review                   |
| • Supervisory Review(s) ( <i>indicate date for each review</i> )  | <input type="checkbox"/> No separate review                   |
| • Pharm/tox review(s), including referenced IND reviews ( <i>indicate date for each review</i> )  | <input type="checkbox"/> None                                 |
| ❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer ( <i>indicate date for each review</i> )   | <input type="checkbox"/> None 2013-04-17                      |
| ❖ Statistical review(s) of carcinogenicity studies ( <i>indicate date for each review</i> )   | <input type="checkbox"/> No carc                              |
| ❖ ECAC/CAC report/memo of meeting   | <input type="checkbox"/> None<br>Included in P/T review, page |
| ❖ OSI Nonclinical Inspection Review Summary ( <i>include copies of OSI letters</i> )  | <input type="checkbox"/> None requested                       |

| <b>Product Quality</b> <input type="checkbox"/> None  |   |
|---|---|
| <b>❖ Product Quality Discipline Reviews</b>   |   |
| • ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>  | <input type="checkbox"/> No separate review   |
| • Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>   | <input type="checkbox"/> No separate review   |
| • Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>   | <input type="checkbox"/> None 2013-03-25; 2013-04-25; 2013-10-10; 2013-10-25; 2013-12-20; 2013-12-23; 2014-06-27; 2014-09-08; 2014-09-11  |
| <b>❖ Microbiology Reviews</b><br><input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i><br><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  |
| <b>❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer</b> <i>(indicate date of each review)</i>   | <input type="checkbox"/> None   |
| <b>❖ Environmental Assessment (check one) (original and supplemental applications)</b>  |   |
| <input checked="" type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>  | 2013-10-10  |
| <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>  |   |
| <b>❖ Facilities Review/Inspection</b>   |   |
| <input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout or EER Summary Report only; do <b>NOT</b> include EER Detailed Report; date completed must be within <b>2 years</b> of action date) <i>(only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites<sup>5</sup>)</i> | Date completed: 2014-08-21<br><input checked="" type="checkbox"/> Acceptable<br><input type="checkbox"/> Withhold recommendation<br><input type="checkbox"/> Not applicable           |
| <input type="checkbox"/> BLAs: TB-EER (date of most recent TB-EER must be within <b>30 days</b> of action date) <i>(original and supplemental BLAs)</i>   | Date completed:<br><input type="checkbox"/> Acceptable<br><input type="checkbox"/> Withhold recommendation  |
| <b>❖ NDAs: Methods Validation</b> <i>(check box only, do not include documents)</i>   | <input checked="" type="checkbox"/> Completed<br><input type="checkbox"/> Requested<br><input type="checkbox"/> Not yet requested<br><input type="checkbox"/> Not needed (per review) |

<sup>5</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.

| Day of Approval Activities   |  |
|--|--|
| ❖ For all 505(b)(2) applications:<br>• Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)   | <input type="checkbox"/> No changes<br><input type="checkbox"/> New patent/exclusivity ( <i>Notify CDER OND IO</i> ) |
| • Finalize 505(b)(2) assessment  | <input type="checkbox"/> Done  |
| ❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email  | <input checked="" type="checkbox"/> Done   |
| ❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter   | <input type="checkbox"/> Done  |
| ❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name | <input checked="" type="checkbox"/> Done   |
| ❖ Ensure Pediatric Record is accurate  | <input checked="" type="checkbox"/> Done   |
| ❖ Send approval email within one business day to CDER-APPROVALS  | <input checked="" type="checkbox"/> Done   |

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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MICHAEL V MONTELEONE  
09/24/2014



NDA 204734

**ACKNOWLEDGE -  
CLASS 1 COMPLETE RESPONSE**

Shire Development, LLC  
Attention: Linda Mota  
Manager, Global Regulatory Affairs  
725 Chesterbrook Blvd  
Wayne, PA 19087

Dear Ms. Mota:

We acknowledge receipt on July 31, 2014, of your July 31, 2014, resubmission to your supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fosrenol (lanthanum carbonate) Oral Powder 750 mg and 1000 mg.

We consider this resubmission a complete, class 1 response to our action letter. Therefore, the user fee goal date is September 30, 2014.

If you have any questions, please call Michael Monteleone, Regulatory Project Manager, at (301) 796-1952.

Sincerely,

*{See appended electronic signature page}*

Edward Fromm, RPh, RAC  
Chief, Project Management Staff  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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EDWARD J FROMM  
08/18/2014



NDA 204734

**GENERAL ADVICE**

Shire Development, LLC  
Attention: Linda Mota  
Manager, Global Regulatory Affairs  
725 Chesterbrook Blvd  
Wayne, PA 19087

Dear Ms. Mota:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Fosrenol.

We also refer to our teleconference on May 15, 2014 to discuss your planned resubmission of NDA 204734. We also refer to your May 30, 2014, submission, containing proposed interim dissolution specification and a proposed Post Marketing Commitment to develop a new dissolution method.

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

1. Your proposal to use the current dissolution method with an acceptance criterion of  $Q = \frac{(b)}{(4)}\%$  at 20 minutes on an interim basis appears acceptable.
2. Pending a final review upon resubmission, your proposed timelines are also acceptable for a Post-Marketing Commitment for submission of a Prior Approval Supplement with a complete report supporting a revised/new dissolution method and corresponding acceptance criteria.
3. A determination regarding the resubmission classification will be made upon receipt. We anticipate your proposed resubmission will be a Class I.

If you have any questions, please call Michael Monteleone, Regulatory Project Manager, at (301) 796-1952.

Sincerely,

*{See appended electronic signature page}*

Norman Stockbridge, MD, PhD  
Director  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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NORMAN L STOCKBRIDGE  
06/30/2014



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

NDA 204734

**MEETING MINUTES**

Shire Development, LLC  
Attention: Linda Mota  
Manager, Global Regulatory Affairs  
725 Chesterbrook Blvd  
Wayne, PA 19087

Dear Ms. Mota:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Fosrenol.

We also refer to the telecon between representatives of your firm and the FDA on May 15, 2014. The purpose of the meeting was to discuss your planned resubmission of NDA 204734.

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

If you have any questions, please call Michael Monteleone, Regulatory Project Manager at (301) 796-1952.

Sincerely,

*{See appended electronic signature page}*

Norman Stockbridge, MD, PhD  
Director  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

Enclosure:  
Meeting Minutes



**FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH**

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**MEMORANDUM OF MEETING MINUTES**

**Meeting Type:** Type C  
**Meeting Category:** Advice

**Meeting Date and Time:** May 15, 2014 9:00am  
**Meeting Location:** Teleconference

**Application Number:** NDA 204734  
**Product Name:** Fosrenol  
**Indication:** reduce serum phosphate in patients with end stage renal disease  
**Sponsor/Applicant Name:** Shire

**Meeting Chair:** Norman Stockbridge, MD, PhD  
**Meeting Recorder:** Michael Monteleone, MS, RAC

**FDA ATTENDEES**

*Division of Cardiovascular and Renal Products*

Norman Stockbridge, MD, PhD Director  
Michael Monteleone, MS, RAC Project Manager

*Division of New Drug Quality Assessment I*

Lyudmila Soldatova, PhD Chemistry Reviewer  
Angelica Dorantes, PhD Biopharmaceutics Team Leader

*Office of Clinical Pharmacology, Division of Clinical Pharmacology I:*

Divya Menon-Andersen, PhD Clinical Pharmacologist

**APPLICANT ATTENDEES**

Daryl Dekarske Vice President, Global Regulatory Affairs  
Sabrina Girty, J.D. Director, Global Regulatory Affairs  
Kristen P. Manion Director, Global Regulatory Affairs (CMC)  
Linda Mota Manager, Global Regulatory Affairs  
Katharine Andrews Director, Global Regulatory Affairs  
Renee Yancey Associate Director, Global Regulatory Affairs (CMC)  
Patrick J. Koestler, Ph.D. Associate Director Pharmaceutical Analysis,  
Pharmaceutical Sciences  
Don Eades, Ph.D. Director Pharmaceutical Analysis, Pharmaceutical Sciences  
David Eshelman, M.S. Manager Pharmaceutical Analysis, Pharmaceutical  
Sciences

Gareth Lilly, Ph.D.  
J. Brian Copley, M.D.

Director , Non-Clinical Development Operations  
Senior Director, Clinical Development and  
Medical Affairs

Steven Troy, M.S.

Senior Director, Clinical Pharmacology and  
Pharmacokinetics

Svetlana Garafola, M.D.

Director, Medical Surveillance & Risk Management

Neil Kanabar

Senior Analytical Scientist,

## 1.0 BACKGROUND

The applicant submitted NDA 204734 for Fosrenol (lanthanum carbonate) Oral Powder on February 28, 2013. The Division issued a Complete Response letter on December 24, 2013. The primary issue discussed in the Complete Response letter related to the dissolution method and supporting Chemistry, Manufacturing and Controls data. The applicant requested a meeting to discuss their proposal for resubmission on April 2, 2014. The Division sent preliminary responses on May 8, 2014 and met with the applicant via tcon on May 15, 2014, the minutes of that meeting are below.

## 2. DISCUSSION

**Question 1:** *Does the Agency agree with the Applicant's plan for dissolution method development leading to implementing a new dissolution specification on release and stability?*

**Response:** Yes, we agree. In addition, your rationale for not conducting dissolution testing of the 750 and 1000 mg strengths in two additional pH-media (pH 4.5 and pH 6.8) is acceptable.

**Discussion at the meeting:** None.

**Question 2:** *Does the Agency agree with the Applicant's plan to provide the updated dissolution method/specification as part of a post approval commitment and submit a Class 1 labeling resubmission now?*

**Response:** No, we do not agree. Your response to our December 24, 2013 Complete Response letter should contain all of the information needed to resolve the issues outlined in that letter. A decision regarding the resubmission classification will be made at the time of receipt; we anticipate your submission will be a Class 2 resubmission.

**Discussion at the meeting:** Discussion opened with the applicant outlining that they had significant experience with this formulation, which is approved in 29 markets and marketed in 12. The applicant affirmed that they are committed to conducting the requested dissolution work, but that they did not believe it should be a barrier to approval.

The Division said that from a regulatory perspective, a resubmission would not be complete unless it contained sufficient information to resolve all items listed in the December 24, 2013 complete response letter.

The Division commented that the method was being requested from a product quality perspective, as a method to ensure quality batch to batch. The Division said that the similarity of the pharmacodynamics has been established.

The applicant said that they understood the Division's concerns regarding the proposed method and asked if a (b) (4) specification would help ease concerns, perhaps a Q of (b) (4)% in 20 minutes in contrast to the Q of (b) (4)% in (b) (4) minutes previously proposed. The applicant was advised to send in a formal proposal for review and that the Division would comment. The applicant was also advised to include in their proposal the post-marketing commitment timelines for completion of a new dissolution method and for collection of sufficient dissolution data to set the final dissolution specification using the new method, should the Division find acceptable the newly proposed interim dissolution specification of Q = (b) (4)% in 20 minutes.

**Question 3:** *Does the Agency agree to grant a waiver from pediatric studies for Fosrenol Oral Powder?*

**Response:** A decision regarding pediatric studies required under PREA will be made at the time of NDA approval in consultation with the Pediatric Review Committee at FDA. At this time, the Division would support your request for a full waiver.

**Discussion at the meeting:** None.

**Question 4:** *Does the Agency agree that the proper country of origin marking for Fosrenol Oral Powder is "Product of Italy"?*

**Response:** No, we do not agree. The manufacturing process for Fosrenol Powder involves the substantial transformation of the active pharmaceutical ingredient (API), Lanthanum Carbonate, at Catalent Germany Schorndorf GmbH. Therefore, the final drug product manufacturer, Catalent Germany Schorndorf GmbH, should be indicated on the carton and container labeling as per requirements by US Customs and Border Protection (CBP). As such, the carton and container labels may include the following statements:

Manufactured for Shire US Inc.,  
Wayne, PA 19087, USA

Manufactured by Catalent Germany Schorndorf GmbH  
D-73614 Shorndorf  
Germany

**Discussion at the meeting:** None.

**Other Important Information**

**DATA STANDARDS FOR STUDIES**

CDER strongly encourages IND sponsors to consider the implementation and use of data standards for the submission of applications for investigational new drugs and product registration. Such implementation should occur as early as possible in the product development lifecycle, so that data standards are accounted for in the design, conduct, and analysis of clinical and nonclinical studies. CDER has produced a web page that provides specifications for sponsors regarding implementation and submission of clinical and nonclinical study data in a standardized format. This web page will be updated regularly to reflect CDER's growing experience in order to meet the needs of its reviewers. The web page may be found at:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm248635.htm>

**LABORATORY TEST UNITS FOR CLINICAL TRIALS**

CDER strongly encourages IND sponsors to identify the laboratory test units that will be reported in clinical trials that support applications for investigational new drugs and product registration. Although Système International (SI) units may be the standard reporting mechanism globally, dual reporting of a reasonable subset of laboratory tests in U.S. conventional units and SI units might be necessary to minimize conversion needs during review. Identification of units to be used for laboratory tests in clinical trials and solicitation of input from the review divisions should occur as early as possible in the development process. For more information, please see [CDER/CBER Position on Use of SI Units for Lab Tests](#).

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/s/  
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NORMAN L STOCKBRIDGE  
05/28/2014

**PeRC PREA Subcommittee Meeting Minutes**  
**October 9, 2013**

**PeRC Members Attending:**

Lynne Yao  
Robert Nelson  
Hari Cheryl Sachs  
Karen Davis-Bruno  
Rosemary Addy  
Patricia Dinndorf  
Julia Pinto  
William J. Rodriguez  
Peter Starke  
Wiley Chambers  
Lily Mulugeta  
Daiva Shetty  
Andrew Mosholder  
Ruthanna Davi  
Barbara Buch  
Martha Nguyen  
Dianne Murphy  
Jane Inglese

**Guests Attending:**

Maura Oleary (CBER)  
Terrie Crescenzi (OPT)  
Nichella Simms (PMHS)  
Erica Radden (PMHS)  
Gilbert Burckart (OCP)  
Donna Snyder (PMHS)  
Melissa Tassinari (PMHS)  
Lawren Slate (OCP)  
Janice Lansita (DAVP)  
Islam Younis (OCP)  
William Tauber (DAVP)  
Linda Lewis (DAVP)  
Jian Wang (OCP)  
Janet Maynard (DPARP)  
Suzette Peng (DPARP)  
Ping Ji (DPARP)  
Satjit Brar (DPARP)  
June Germain (DTOP)  
William Boyd (DTOP)  
Dongliang Zhuang (OB)  
Martin Nevit (DTOP)

Gordana Diglisic (DDDP)  
Melinda McCord (DDDP)  
Gerlie Gieser (OTS/OCP)  
Divya Memon-Andersen (OCP)  
Melanie Blank (DCRP)  
Elizabeth Hausner (DCRP)  
Michael Monteleone (DCRP)

**Agenda**

10:45 NDA  
NDA  
NDA

(b) (4)

204308 Fosrenol (lanthanum carbonate) Full Waiver

(b) (4)

**Fosrenol (lanthanum carbonate) Full Waiver**

- NDA 204308 seeks marketing approval for Fosrenol (lanthanum carbonate) for reducing serum phosphate in patients with end stage renal disease.
- The application was submitted on February 28, 2013, and has a PDUFA goal date of December 28, 2013.
- The application triggers PREA as directed to a new dosage form.
- A full waiver is being requested because the product fails to represent a meaningful therapeutic benefit over existing therapies for pediatric patients and is unlikely to be used in a substantial number of pediatric patients.
- *Division justification for waiver:* There are other drugs (with and without calcium) that are used commonly for phosphate lowering in the pediatric population, including Renvela (sevelamer carbonate) that is a liquid formulation and can be easily titrated. There is an ongoing pediatric study with Renvela. Furthermore, there are other new drugs being developed for hyperphosphatemia that will be required to do pediatric studies. In addition, inconclusive juvenile animal studies do not support the safety of lanthanum in children. Some investigators/ IRBs might consider studying lanthanum in children unethical because there are other effective options that do not pose concerns for developing bone. Finally, there is a relatively small pediatric ESRD population, and it might be considered a better use of resources to enroll them in studies where there is more potential for benefit and less potential for risk.

*PeRC Recommendations:*

- The PeRC disagreed with a full waiver and recommended deferred studies for pediatric patients aged 0 to less than 17 years. The PeRC recommended that deferred studies include an appropriately designed nonclinical study to evaluate bone safety issues. The DCRP pharmtox team will develop a PMR to address this. The PeRC also recommended that pediatric studies be deferred to allow for completion of the nonclinical studies and review of PREA requirements already established for other currently available products for this indication (non-calcium based phosphate binder).

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/s/  
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JANE E INGLESE  
10/21/2013

**From:** Knight, Yvonne  
**To:** ["sgirty@shire.com"](mailto:sgirty@shire.com)  
**Cc:** [Knight, Yvonne](#)  
**Subject:** Product Label Comment for NDA 204734  
**Date:** Thursday, September 12, 2013 7:30:00 AM  
**Importance:** High

---

Good morning Ms. Girty,

The Agency has the following comment in regards to Shire's Product Label for NDA 204734.

"Comment for Foil and Carton Labels:

Include an asterisk at the dosage strength of 750 mg or 1000 mg, and provide the equivalence statement in the smaller font on the side panel or under the dosage strength as follows: "Each stick pack contains 1431 mg lanthanum carbonate equivalent to 750 mg lanthanum", or "Each stick pack contains 1908 mg lanthanum carbonate equivalent to 1000 mg lanthanum", respectively."

Please feel free to contact me if you have any questions.

Regards,

Yvonne Knight, MS  
Regulatory Health Project Manager  
Division of New Drug Quality Assessment  
FDA/CDER/OPS/ONDQA  
10903 New Hampshire Avenue  
Bldg. 21, Room 2667  
Silver Spring, MD 20993-0002  
Phone: 301.796.2133  
Email: [yvonne.knight@fda.hhs.gov](mailto:yvonne.knight@fda.hhs.gov)

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/s/  
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YVONNE L KNIGHT  
09/12/2013



NDA 204734

## INFORMATION REQUEST

Shire Development, LLC  
Attention: Sabrina R. Girty, JD  
Director, Global Regulatory Affairs  
725 Chesterbrook Blvd  
Wayne, PA 19087

Dear Ms. Girty:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fosrenol (lanthanum carbonate) Oral Powder 750 mg and 1000 mg.

We also refer to your February 28, 2013, submission.

We are reviewing the Quality section of your submission and have the following comments and information requests. We request a written response by September 9, 2013, in order to continue our evaluation of your NDA.

1.  (b) (4)
2.  (b) (4)
3. The 24-month long-term stability data provided for two primary stability batches of each dosage strength is not sufficient to grant the expiration dating period for drug product. Provide the updated 12-month long-term stability data for three commercial scale batches of each dosage strengths that were manufactured in November/December 2011 and packaged in the commercial stick packs (23 mm x 80 mm). Include dissolution testing for the currently ongoing three stability batches. Collect dissolution profile data.
4. The rationale you have provided for excluding *in-vitro* drug release testing from the drug product specifications is not acceptable. One of the crucial quality tests for oral solid dosage forms, including powders and multi-particulate dosage forms in general, is *in-vitro* drug release characterization. Although not absorbed into the systemic circulation,

lanthanum carbonate must go into solution for binding of phosphate to occur. Therefore, provide a proposal for the implementation of dissolution as QC test for product release and stability testing, and provide updated drug product specification. Provide the report for the proposed dissolution method and include the dissolution multi-point profile data for the bio-batches and registration batches.

5. Your rationale for not providing comparative dissolution data for the 750 and 1000 mg dosage strengths of your proposed product in support of your biowaiver request is not acceptable. For the approval of the biowaiver request of the lower strength the following additional requirements should be met: acceptable in vitro multi-point dissolution profile comparison and f2 data in 3 different pH media using the same dissolution testing conditions. Provide this supportive information.
6. The proposed annual stability commitment is not acceptable. You should place one batch of each dose strength of drug product, 750 mg and 1000 mg, per year on long-term stability (25°C/60%RH) in the commercial packs according to the proposed stability protocol.
7. Include microbiological testing in the Stability Testing Protocol for Annual Stability Batches.
8. You stated in the Dosage and Administration section of the Package Insert that FOSRENOL Oral Powder should be consumed immediately ( (b) (4) ) after mixing with a soft food. What is the basis of this statement regarding the (b) (4) time frame of consumption.

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

Sincerely,

*{See appended electronic signature page}*

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

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/s/  
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RAMESH K SOOD  
08/08/2013



NDA 204734

**FILING COMMUNICATION**

Shire Development, LLC  
Attention: Sabrina R. Girty, JD  
Director, Global Regulatory Affairs  
725 Chesterbrook Blvd  
Wayne, PA 19087

Dear Ms. Girty:

Please refer to your New Drug Application (NDA) dated February 28, 2013, received February 28, 2013, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act, for Fosrenol (lanthanum carbonate) Oral Powder 750 mg and 1000 mg.

We also refer to your amendments dated March 15 and April 10, 2013.

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 28, 2013.

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 November 28, 2013.

We request that you submit the following information:

1. In the phase 1 clinical trial, 240 cc of water was administered after each dose of lanthanum powder and not after the tablet. Please provide the rationale for conducting the trial this way and please provide a rationale for why you believe that administering the drug without any specifications regarding water as you currently propose in the label will not affect safety, tolerability or effectiveness.

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

Under **HIGHLIGHTS**:

1. The length of HL must be less than or equal to one-half page (the HL Boxed Warning does not count against the one-half page requirement) unless a waiver has been granted in a previous submission (i.e., the application being reviewed is an efficacy supplement).

*Advice: Reduce HL length to one-half page.*

2. Recent Major Changes (RMC) pertains to only the following five sections of the FPI: Boxed Warning, Indications and Usage, Dosage and Administration, Contraindications, and Warnings and Precautions.

*Advice: Remove Dosage Forms and Strengths from RMC.*

Under **TABLE OF CONTENTS**:

3. If a section or subsection from 201.56(d)(1) is omitted from the FPI and TOC, the heading “**FULL PRESCRIBING INFORMATION: CONTENTS**” must be followed by an asterisk and the following statement must appear at the end of TOC: “\*Sections or subsections omitted from the Full Prescribing Information are not listed.”

*Advice: Capitalize ‘Full Prescribing Information’.*

Under **FULL PRESCRIBING INFORMATION**:

4. When postmarketing adverse reaction data is included (typically in the “Postmarketing Experience” subsection of Adverse Reactions), the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

*“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.”*

*Advice: Add statement to section 6.2, Postmarketing Experience.*

We request that you resubmit labeling that addresses these issues by May 20, 2013. The resubmitted labeling will be used for further labeling discussions.

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.

## **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, please call Michael Monteleone, Regulatory Project Manager, at (301) 796-1952.

Sincerely,

*{See appended electronic signature page}*

Norman Stockbridge, MD, PhD  
Director  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

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/s/  
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NORMAN L STOCKBRIDGE  
04/29/2013



NDA 204734

**NDA ACKNOWLEDGMENT**

Shire Development, LLC  
Attention: Sabrina R. Girty, JD  
Director, Global Regulatory Affairs  
725 Chesterbrook Blvd  
Wayne, PA 19087

Dear Ms. Girty:

We have received your New Drug Application (NDA) submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Fosrenol (lanthanum carbonate) Oral Powder 750 mg and 1000 mg

Date of Application: February 28, 2013

Date of Receipt: February 28, 2013

Our Reference Number: NDA 204734

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, 2013, 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).

Title VIII of FDAAA amended the PHS Act by adding new section 402(j) [42 USC § 282(j)], which expanded the current database known as ClinicalTrials.gov to include mandatory

registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices.

In addition to the registration and reporting requirements described above, FDAAA requires that, at the time of submission of an application under section 505 of the FDCA, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been met. Where available, the certification must include the appropriate National Clinical Trial (NCT) numbers [42 USC § 282(j)(5)(B)].

You did not include such certification when you submitted this application. You may use Form FDA 3674, "Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank," [42 U.S.C. § 282(j)] to comply with the certification requirement. The form may be found at <http://www.fda.gov/opacom/morechoices/fdaforms/default.html>.

In completing Form FDA 3674, you should review 42 USC § 282(j) to determine whether the requirements of FDAAA apply to any clinical trial(s) referenced in this application. Please note that FDA published a guidance in January 2009, "Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of the Food and Drug Administration Amendments Act of 2007," that describes the Agency's current thinking regarding the types of applications and submissions that sponsors, industry, researchers, and investigators submit to the Agency and accompanying certifications. Additional information regarding the certification form is available at:

<http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA/ct/SignificantAmendmentstotheFDCAAct/FoodandDrugAdministrationAmendmentsActof2007/ucm095442.htm>. Additional information regarding Title VIII of FDAAA is available at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>. Additional information for registering your clinical trials is available at the Protocol Registration System website <http://prsinfo.clinicaltrials.gov/>.

When submitting the certification for this application, **do not** include the certification with other submissions to the application. Submit the certification within 30 days of the date of this letter. In the cover letter of the certification submission clearly identify that it pertains to **NDA 204734** submitted on February 28, 2013, and that it contains the FDA Form 3674 that was to accompany that application.

If you have already submitted the certification for this application, please disregard the above.

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 Cardiovascular and Renal 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>.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to [SecureEmail@fda.hhs.gov](mailto:SecureEmail@fda.hhs.gov). Please note that secure email may not be used for formal regulatory submissions to applications.

If you have any questions, please call Michael Monteleone, Regulatory Project Manager, at (301) 796-1952.

Sincerely,

*{See appended electronic signature page}*

Edward Fromm, RPh, RAC  
Chief, Project Management Staff  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

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/s/  
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EDWARD J FROMM  
03/14/2013

|   |   |  |   |  |  |
|---|---|--|---|--|--|
| Form Approved: OMB No. 0910 - 0297 Expiration Date: January 31, 2013. See instructions for OMB Statement, below.  |   |  |   |  |  |
| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>FOOD AND DRUG ADMINISTRATION   | <b>PRESCRIPTION DRUG USER FEE COVERSHEET</b>  |  |   |  |  |
| <p>A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on FDA's website:<br/> <a href="http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm">http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm</a></p>   |   |  |   |  |  |
| 1. APPLICANT'S NAME AND ADDRESS<br><br>SHIRE US INC<br>Linda Mota<br>725 Chesterbrook Blvd.<br>Wayne PA 19087-5637<br>US  | 4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER<br><br>204-734   |  |   |  |  |
| 2. NAME AND TELEPHONE NUMBER OF REPRESENTATIVE<br>484-595-8397  | 5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?<br><input type="checkbox"/> YES <input checked="" type="checkbox"/> NO<br><br>IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:<br><br><input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION<br><br><input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO: |  |   |  |  |
| 3. PRODUCT NAME<br>Fosrenol ( Lanthanum Carbonate )   | 6. USER FEE I.D. NUMBER<br>PD3012960  |  |   |  |  |
| 7. ARE YOU REDEEMING A PRIORITY REVIEW VOUCHER FOR THE TREATMENT OF TROPICAL DISEASES? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO<br><br>PRIORITY REVIEW VOUCHER NUMBER:   |   |  |   |  |  |
| 8. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.<br><input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)<br><input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act<br><input checked="" type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY  |   |  |   |  |  |
| 9. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO<br>If a waiver has been granted, include a copy of the official FDA notification with your submission.   |   |  |   |  |  |
| OMB Statement:<br>Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:<br><br><table style="width:100%; border: none;"> <tr> <td style="width: 33%; border: none;">                             Department of Health and Human Services<br/>                             Food and Drug Administration<br/>                             Center for Biologics Evaluation and Research<br/>                             Office of Information Management (HFA-710)<br/>                             1350 Piccard Drive, 4th Floor<br/>                             Rockville, MD 20850                         </td> <td style="width: 33%; border: none;">                             Department of Health and Human Services<br/>                             Food and Drug Administration<br/>                             Center for Drug Evaluation and Research<br/>                             Office of Information Management (HFA-710)<br/>                             1350 Piccard Drive, 4th Floor<br/>                             Rockville, MD 20850                         </td> <td style="width: 33%; border: none;">                             An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.                         </td> </tr> </table> |   |  | Department of Health and Human Services<br>Food and Drug Administration<br>Center for Biologics Evaluation and Research<br>Office of Information Management (HFA-710)<br>1350 Piccard Drive, 4th Floor<br>Rockville, MD 20850 | Department of Health and Human Services<br>Food and Drug Administration<br>Center for Drug Evaluation and Research<br>Office of Information Management (HFA-710)<br>1350 Piccard Drive, 4th Floor<br>Rockville, MD 20850 | An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. |
| Department of Health and Human Services<br>Food and Drug Administration<br>Center for Biologics Evaluation and Research<br>Office of Information Management (HFA-710)<br>1350 Piccard Drive, 4th Floor<br>Rockville, MD 20850   | Department of Health and Human Services<br>Food and Drug Administration<br>Center for Drug Evaluation and Research<br>Office of Information Management (HFA-710)<br>1350 Piccard Drive, 4th Floor<br>Rockville, MD 20850  | An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. |   |  |  |
| PRINTED NAME AND SIGNATURE OF AUTHORIZED REPRESENTATIVE<br>   | TITLE<br>Director, RA   | DATE<br>2/14/2013  |   |  |  |
| 9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION<br>\$979,400.00   |   |  |   |  |  |
| Form FDA 3397 (01/10)   |   |  |   |  |  |



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

NDA 204734

MEETING PRELIMINARY COMMENTS

Shire Development LLC  
Attention: Sabrina R. Girty, JD  
Director, Global Regulatory Affairs  
725 Chesterbrook Blvd  
Wayne, PA, 19087

Dear Ms. Girty:

Please refer to your Pre-New Drug Application (NDA) for Fosrenol (lanthanum carbonate) 750 mg and 1000 mg powder.

We also refer to your August 30, 2012, correspondence, requesting a meeting to discuss your planned NDA submission.

Our preliminary responses to your meeting questions are enclosed.

If you have any questions, please call Michael Monteleone, Regulatory Project Manager, at (301) 796-1952.

Sincerely,

*{See appended electronic signature page}*

Norman Stockbridge, MD, PhD  
Director  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

ENCLOSURE:  
Preliminary Meeting Comments

## PRELIMINARY MEETING COMMENTS

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

**Meeting Date and Time:** Cancelled  
**Meeting Location:** Cancelled

**Application Number:** NDA 204734  
**Product Name:** lanthanum carbonate  
**Indication:** reduce serum phosphate in patients with end stage renal disease  
**Sponsor/Applicant Name:** Shire

### Introduction:

This material consists of our responses to your questions and any additional comments. We believe that these responses adequately address the issues and so we are cancelling our meeting scheduled for November 13, 2012.

### 1.0 BACKGROUND

The Sponsor and Division met previously to discuss concerns regarding tablet hardness and complications such as tooth injury, aspiration, and GI obstruction resulting from Fosrenol chewable tablets being inadequately chewed. Subsequent to these discussions, the Sponsor amended the labeling and implemented a Medication Guide for Fosrenol Chewable Tablets to include instructions that tablets may be crushed before chewing to address the concerns. The Division and Sponsor also discussed potential alternative formulations.

On August 30, 2012 the sponsor requested a Pre-NDA meeting to discuss their planned submission of an NDA for a powder formulation of Fosrenol.

### 2.0 DISCUSSION

***Question 1:** Shire plans to provide a cross-reference to NDA 021468 for drug substance information supporting the oral powder formulation. Does the Agency agree?*

**Response:** It is acceptable to reference the drug substance section of the approved Fosrenol (lanthanum carbonate) Chewable Tablets NDA for all relevant CMC information.

***Question 2:** Shire plans to provide a cross-reference to NDA 021468 for safety and efficacy information supporting the oral powder formulation and plans to submit a combined package insert for the chewable tablet and oral powder formulations. Does the Agency agree?*

**Response:** Yes. You should also submit safety information from the current worldwide marketing experience with these formulations.

**Question 3:** *Shire's scientific rationale concludes that further in vivo or in vitro comparison testing to support the biowaiver for Fosrenol (lanthanum carbonate) 750mg Oral Powder is not required. Does the Agency agree?*

**Response:** Yes.

**Question 4:** *It is Shire's position that the proper dosage form designation for this formulation is Fosrenol (lanthanum carbonate) Oral Powder. Does the Agency agree?*

**Response:** The designation of the new formulation as Fosrenol (lanthanum carbonate) Oral Powder is tentatively acceptable pending evaluation of all information to be submitted in the NDA.

**Question 5:** *Shire seeks any Agency "General Advice" comments whether the proposed body of clinical and quality information is adequate to support the filing of the NDA and whether any additional information is considered necessary by the Agency for incorporation into the NDA prior to its submission.*

**Response:** We note that systemic lanthanum exposures appear to be higher with the oral powder formulation than with the tablet formulation. This will likely be a review issue. You will also need to address PREA requirements in your submission.

### 3.0 OTHER COMMENTS

#### PREA PEDIATRIC STUDY PLAN

The Food and Drug Administration Safety and Innovation Act of 2012 changes the timeline for submission of a PREA Pediatric Study Plan and includes a timeline for the implementation of these changes. You should review this law and assess if your application will be affected by these changes. If you have any questions, please email the Pediatric Team at [Pedsdrugs@fda.hhs.gov](mailto:Pedsdrugs@fda.hhs.gov).

#### PRESCRIBING INFORMATION

Proposed prescribing information (PI) submitted with your 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/LawsActsandRules/ucm084159.htm>. We encourage you to review the information at this website and use it as you draft prescribing information for your application.

**MANUFACTURING FACILITIES**

To facilitate our inspectional process, the Office of Manufacturing and Product Quality in CDER's Office of Compliance requests that you 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.        |              |                                |                      |               |

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

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NORMAN L STOCKBRIDGE  
11/06/2012