

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205109Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

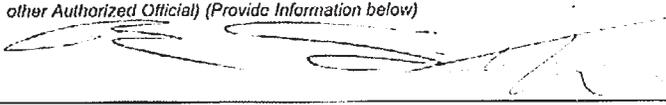
1.3.5.1 Patent Information

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 <i>For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use</i>		NDA NUMBER 205109	
		NAME OF APPLICANT/NDA HOLDER Vifor Fresenius Medical Care Renal Pharma France	
<i>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</i>			
TRADE NAME (OR PROPOSED TRADE NAME) Pending			
ACTIVE INGREDIENT(S) Mixture of polynuclear iron(III)-oxyhydroxide, sucrose, and starches		STRENGTH(S) 500 mg iron(III)	
DOSAGE FORM chewable tablets			
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 <i>only</i> 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 6,174,442		b. Issue Date of Patent 16th January, 2001	c. Expiration Date of Patent 19th December, 2016
d. Name of Patent Owner Vifor (International) AG		Address (of Patent Owner) Rechenstrasse 37	
		City/State St. Gallen, Switzerland	
		ZIP Code CH-9014	FAX Number (if available)
		Telephone Number +41.58.851.80.00	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 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States) Jules Jay Morris SVP, Deputy General Counsel for Intellectual Property		Address (of agent or representative named in 1.e.) 920 Winter St	
		City/State Waltham/MA	
		ZIP Code 02451	FAX Number (if available) 781-699-9410
		Telephone Number 781-699-9129	E-Mail Address (if available) Jay.Morris@fmc-na.com
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes <input type="checkbox"/> No	

FORM FDA 3542a (10/10)

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?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> 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?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> 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).	<input type="checkbox"/> Yes <input type="checkbox"/> 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.)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
2.6 Does the patent claim only an intermediate?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> 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.)	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> 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?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
3.2 Does the patent claim only an intermediate?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> 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.)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
4. Method of Use	
<i>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:</i>	
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?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
4.2 Patent Claim Number(s) (as listed in the patent) 9,10,11,12,13,14	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? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> 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.) Phosphate binder. Control of serum phosphorus levels in patients with end stage renal disease
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.	<input type="checkbox"/> Yes

6. Declaration Certification	
<p>6.1 <i>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.</i></p> <p>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</p>	
6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)	Date Signed
	12/12/2012
<p>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).</p>	
<p>Check applicable box and provide information below.</p>	
<input type="checkbox"/> NDA Applicant/Holder	<input type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input checked="" type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Behruz Fslami and Jean -Marc Ligibel	
Address Vifor Pharma Ltd. Flughofstrasse 61	City/State Glattbrugg Switzerland
ZIP Code CH-8152	Telephone Number +41 58 851 8020 or +41 58 851 82 85
FAX Number (if available)	E-Mail Address (if available)
<p>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:</p> <p style="text-align: center;">Department of Health and Human Services Food and Drug Administration Office of Chief Information Officer 1350 Piccard Drive, Room 400 Rockville, MD 20850</p> <p style="text-align: center;"><i>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.</i></p>	

EXCLUSIVITY SUMMARY

NDA # 205109

SUPPL #

HFD # 110

Trade Name Velphoro

Generic Name (b) (4)

Applicant Name Vifor Fresenius Medical Care Renal Pharma

Approval Date, If Known November 27, 2013

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES NO

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

505(b)(1)

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

YES NO

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

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

d) Did the applicant request exclusivity?

YES NO

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

5

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# 20955 Ferrlecit (sodium ferric gluconate complex in sucrose injection)
NDA# 17441 INFed (Iron dextran)
NDA# 40024 Dexferrum (iron dextran injection)

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 PA-CL-05A/05B and PA-CL-03A

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"):

Study PA-CL-03A, phase 2, fixed dose efficacy and safety study

Study PA-CL-05A/05B, phase 3, pivotal, dose titration and randomized withdrawal study

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 # 75610 YES ! NO
! Explain:

Investigation #2
IND # 75610 YES ! NO
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

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

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

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

YES NO

If yes, explain:

Name of person completing form: Anna Park
Title: Senior Regulatory Project Manager
Date: December 5, 2013

Name of Office/Division Director signing form: Norman Stockbridge, M.D., Ph.D.
Title: Division Director

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

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

/s/

ANNA J PARK
12/05/2013

NORMAN L STOCKBRIDGE
12/05/2013

1.9.1 Request for Waiver of Pediatric Studies

Product name: Proposed trade names [REDACTED]^{(b) (4)} Velphoro

Company code: PA21

NDA number: 205109

Applicant: Vifor Fresenius Medical Care Renal Pharma France

Proposed Indication: PA21 is a phosphate binder indicated for the control of serum phosphorus in patients with End Stage Renal Disease.

Vifor Fresenius Medical Care Renal Pharma France is not requesting a waiver under section 505B(a)(4)(B) of the Federal Food, Drug, and Cosmetic Act (Act).

1.9.2 Request for Deferral of Pediatric Studies

Product name: Proposed trade names (b) (4) Velphoro

Company code: PA21

NDA number: 205109

Applicant: Vifor Fresenius Medical Care Renal Pharma France

Proposed Indication: PA21 is a phosphate binder indicated for the control of serum phosphorus in patients with End Stage Renal Disease (ESRD).

The initial pediatric study plan for PA21 was previously submitted to IND 075610 (SN0033), in which the (b) (4)

As recommended in the Agency's response letter dated November 3, 2010, "Pediatric studies should be delayed until after the safety and effectiveness of your drug has been established in the adult population and age-appropriate formulations are available".

Therefore, Vifor Fresenius Medical Care Renal Pharma France hereby requests a deferral of pediatric studies for PA21 under Section 505B(a)(3) of the Federal Food, Drug and Cosmetic Act (the Act). The sponsor is open to discuss an appropriate pediatric development plan after the safety and effectiveness of PA21 has been established, as well as subject of NDA approval.

1.3.3 Debarment Certification



DEBARMENT CERTIFICATION

RE: New Drug Application for PA21

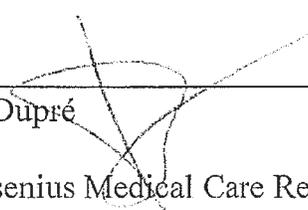
NDA#: 205109

NDA Sponsor: Vifor Fresenius Medical Care Renal Pharma France

US Agent: Fresenius Medical Care North America

Vifor Fresenius Medical Care Renal Pharma France 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.

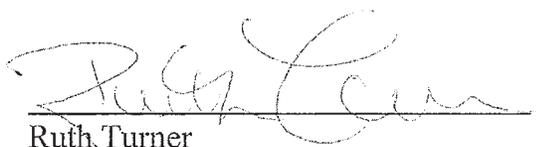
Certified on behalf of the NDA Sponsor
Vifor Fresenius Medical Care Renal Pharma France



Florence Dupré
President
Vifor Fresenius Medical Care Renal Pharma France

17/12/2012
Date

Certified on behalf of the US Agent
Fresenius Medical Care North America



Ruth Turner
Director, Regulatory Affairs - Pharma
Fresenius Medical Care North America

18 DEC 2012
Date

1.3.4 FDA Form 3454

DEPARTMENT OF HEALTH AND HUMAN SERVICES Food and Drug Administration CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS	Form Approved: OMB No. 0910-0396 Expiration Date: August 31, 2012						
<i>TO BE COMPLETED BY APPLICANT</i>							
With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).							
<div style="border: 1px solid black; padding: 2px; display: inline-block;"> Please mark the applicable checkbox. </div>							
<input type="checkbox"/> (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).							
Clinical Investigators	<table border="1" style="width:100%; border-collapse: collapse;"> <tr><td style="height: 20px;"> </td><td style="width: 20px;"> </td></tr> <tr><td style="height: 20px;"> </td><td> </td></tr> <tr><td style="height: 20px;"> </td><td> </td></tr> </table>						
<input checked="" type="checkbox"/> (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).							
<input type="checkbox"/> (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.							
<table border="1" style="width:100%; border-collapse: collapse;"> <tr> <td style="width: 50%; padding: 2px;"> NAME Florence Dupre </td> <td style="width: 50%; padding: 2px;"> TITLE President VFMCRP France </td> </tr> <tr> <td colspan="2" style="padding: 2px;"> FIRM/ORGANIZATION Vifor Fresenius Medical Care Renal Pharma France (VFMCRP France) </td> </tr> <tr> <td style="padding: 2px;"> SIGNATURE </td> <td style="padding: 2px;"> DATE (mm/dd/yyyy) 12/12/2012 </td> </tr> </table>		NAME Florence Dupre	TITLE President VFMCRP France	FIRM/ORGANIZATION Vifor Fresenius Medical Care Renal Pharma France (VFMCRP France)		SIGNATURE 	DATE (mm/dd/yyyy) 12/12/2012
NAME Florence Dupre	TITLE President VFMCRP France						
FIRM/ORGANIZATION Vifor Fresenius Medical Care Renal Pharma France (VFMCRP France)							
SIGNATURE 	DATE (mm/dd/yyyy) 12/12/2012						
Paperwork Reduction Act Statement							
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. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right.	Department of Health and Human Services Food and Drug Administration Office of Chief Information Officer 1350 Piccard Drive, 420A Rockville, MD 20850						

FORM FDA 3454 (10/09)

PSC Graphics (201) 443-1000 EF

42 Pages have been Withheld in Full as b4 (CCI/TS)
 immediately following this page.

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 205109 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type:
Proprietary Name: Velphoro Established/Proper Name: (b) (4) Dosage Form: tablet		Applicant: Vifor Fresenius Medical Care Renal Pharma Agent for Applicant (if applicable):
RPM: Anna Park		Division: Division of Cardiovascular and Renal Products
<p><u>NDA and NDA Efficacy Supplements:</u></p> <p>NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>	<p><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></p> <p>Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> This application does not rely upon a listed drug. <input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> This application relies on (explain)</p> <p><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check:</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p>	
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is December 1, 2013 	<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR	
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 	<input checked="" type="checkbox"/> None	

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

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

<p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____</p>	<input type="checkbox"/> Received
<p>❖ Application Characteristics ³</p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</p> <p> <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC <input type="checkbox"/> Breakthrough Therapy designation </p> <p> NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies </p> <p> <input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request </p> <p> BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies </p> <p> REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Communication Plan <input type="checkbox"/> ETASU <input type="checkbox"/> MedGuide w/o REMS <input type="checkbox"/> REMS not required </p> <p>Comments:</p>	
<p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p>	<input type="checkbox"/> Yes, dates
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> Press Office notified of action (by OEP) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	<input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

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

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

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

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

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

Yes No

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

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

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

Yes No

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

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

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

Yes No

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

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

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

Yes No

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

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

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

❖ Copy of this Action Package Checklist ⁴	included
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) Approval on November 27, 2013
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	11/26/2013
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	2/1/2013
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	

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

<ul style="list-style-type: none"> ❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>) 	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	
<ul style="list-style-type: none"> ❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>) 	
<ul style="list-style-type: none"> • Most-recent draft labeling 	11/26/2013
<ul style="list-style-type: none"> ❖ Proprietary Name <ul style="list-style-type: none"> • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) • Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name. 	Acceptability 9/16/2013 6/7/2013 & 9/16/2013
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input checked="" type="checkbox"/> RPM 4/16/2013 <input checked="" type="checkbox"/> DMEPA 10/5/2013 <input type="checkbox"/> DMPP/PLT (DRISK) <input checked="" type="checkbox"/> OPDP (DDMAC) 11/22/2013 <input checked="" type="checkbox"/> SEALD 11/22/2013 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
<ul style="list-style-type: none"> ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁵/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>) 	04/16/2013; Biopharm: 3/25/13; Cherry 3/25/13; Clin Pharm; 3/15/13; Clinical: 3/15/13; CMC; 3/12/13 <input type="checkbox"/> Not a (b)(2) <input type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm 	
<ul style="list-style-type: none"> • Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <u>10/30/2013</u> If PeRC review not necessary, explain: _____ • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input checked="" type="checkbox"/> Included

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

❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent <i>(include certification)</i>	<input type="checkbox"/> Verified, statement is acceptable
❖ Outgoing communications <i>(letters, including response to FDRR (do not include previous action letters in this tab), emails, faxes, telecons)</i>	
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• Regulatory Briefing <i>(indicate date of mtg)</i>	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting <i>(indicate date of mtg)</i>	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> No mtg 9/19/2012
• EOP2 meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> No mtg 3/31/2010
• Other milestone meetings (e.g., EOP2a, CMC pilots) <i>(indicate dates of mtgs)</i>	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available <i>(do not include transcript)</i>	
Decisional and Summary Memos	
❖ Office Director Decisional Memo <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Division Director Summary Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 11/27/2013
Cross-Discipline Team Leader Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 11/08/2013
PMR/PMC Development Templates <i>(indicate total number)</i>	<input type="checkbox"/> None 1
Clinical Information⁶	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) <i>(indicate date for each review)</i>	10/11/2013; concur
• Clinical review(s) <i>(indicate date for each review)</i>	10/10/2013
• Social scientist review(s) (if OTC drug) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not <i>(indicate date of review/memo)</i>	
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management	
• REMS Documents and REMS Supporting Document <i>(indicate date(s) of submission(s))</i>	
• REMS Memo(s) and letter(s) <i>(indicate date(s))</i>	
• Risk management review(s) and recommendations (including those by OSE and CSS) <i>(indicate date of each review and indicate location/date if incorporated into another review)</i>	<input checked="" type="checkbox"/> None

⁶ Filing reviews should be filed with the discipline reviews.

❖ OSI Clinical Inspection Review Summary(ies) (include copies of OSI letters to investigators)	<input type="checkbox"/> None requested 10/11/2013
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None 9/21/2013; concur
Statistical Review(s) (indicate date for each review)	<input type="checkbox"/> None 9/20/2013
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None 10/22/2013 ; concur
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None 10/22/2013
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of OSI letters)	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Supervisory Review(s) (indicate date for each review)	<input type="checkbox"/> None 10/8/2013 & 4/25/2013; concur
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None 10/7/2013 & 4/25/2013
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input type="checkbox"/> None 4/3/2013 Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary (include copies of OSI letters)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Branch Chief/Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None 11/7/2013 & 9/27/2013; concur
• Product quality review(s) including ONDQA biopharmaceutics reviews (indicate date for each review)	<input type="checkbox"/> None 11/7/2013 & 9/27/2013
❖ Microbiology Reviews	<input checked="" type="checkbox"/> Not needed
<input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (indicate date of each review)	
<input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) (indicate date of each review)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)	<input type="checkbox"/> None

❖ Environmental Assessment (check one) (original and supplemental applications)		
<input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)		9/27/13
<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)		
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)		
❖ Facilities Review/Inspection		
<input type="checkbox"/> NDAs: Facilities inspections (include EER printout or EER Summary Report only; do NOT include EER Detailed Report) (<i>date completed must be within 2 years of action date</i>) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁷</i>)		Date completed: 10/2/2013 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) (<i>original and supplemental BLAs</i>)		Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>)		<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

⁷ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

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

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

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

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

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

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

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

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

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

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

/s/

ANNA J PARK
12/05/2013

MEMORANDUM

To: NDA 205-109
From: Thomas M. Wong, Ph.D., Chemist
Date: Nov 7, 2013
Drug: Velphoro™ (Suroferric oxyhydroxide) Chewable Tablets
Route of administration: Oral
Strength: 500 mg
Subject: “Approval” recommendation for NDA 205-109

The pending dissolution specification issue mentioned in the CMC Review #1 has now been resolved. The biopharmaceutics reviewer has accepted the original proposed dissolution acceptance criterion of $Q = \text{(b) (4)}$ in 45 minutes (see the biopharmaceutics reviewer Dr. Chikhale’s approval recommendation memo in DARRTS dated Nov 7, 2013).

CMC Recommendation:

The application is recommended for “Approval” from CMC perspective.

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

/s/

THOMAS M WONG
11/07/2013

OLEN M STEPHENS
11/07/2013



NDA 205109

Vifor Fresenius Medical Care Renal Pharma France
Attention: Ms. Florence Dupre
President of VFMCRP France
7-13, Boulevard Paul-Emile Victor
92521 Neuilly-sur-Seine, France

Dear Ms. Dupre:

We acknowledge your October 18, 2013 correspondence notifying the Food and Drug Administration (FDA) that the corporate address has been changed from

12 Rue de la Chaussee d' Antin
75009 Paris, France

to

7-13, Boulevard Paul-Emile Victor
92521 Neuilly-sur-Seine, France

for NDA 205109 for PA21 [REDACTED] ^{(b) (4)} Chewable Tablets, 500 mg.

We have revised our records to reflect this change.

Please cite the NDA number listed above 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

If you have any questions, please contact:

Anna Park, R.Ph., RAC
Regulatory Health Project Manager
(301) 796-1129

Sincerely,

{See appended electronic signature page}

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

cc: Fresenius Medical Care North America
Attention: Ms. Ruth Turner
U.S. Agent for Vifor Fresenius Medical Care Renal Pharma
Director, Regulatory Affairs Pharmaceuticals
920 Winter Street
Waltham, MA 02451

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/s/

EDWARD J FROMM
10/24/2013

Bouie, Teshara

From: Bouie, Teshara
Sent: Tuesday, October 22, 2013 9:26 AM
To: ruth.s.turner@fmc-na.com; Joy Wei (Joy.Weil@fmc-na.com)
Cc: Park, Anna
Subject: NDA 205109

Hi Ruth/Joy,

We have reviewed your submission dated Oct 16, 2013, and determined that the provided data support the approval of your originally proposed dissolution acceptance criterion of $Q=(b)(4)$ at 45 minutes as discussed and agreed on Sept 25, 2013, during our teleconference. Alternatively you can set the dissolution acceptance criterion at $Q=(b)(4)$ at 60 minutes.

We request that you provide a revise drug product specification table accordingly.

Regards,

Teshara G. Bouie, MSA, OTR/L
CDR, United States Public Health Service
Regulatory Health Project Manager
FDA/CDER/OPS/ONDQA
Division of New Drug Quality Assessment I
Phone (301) 796-1649
Fax (301) 796-9749

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/s/

TESHARA G BOUIE
10/22/2013



NDA 205109

GENERAL ADVICE

Vifor Fresenius Medical Care Renal Pharma
Attention: Ms. Florence Dupre
President of VFMCRP France
12, Rue de la Chaussée d'Antin
Paris, France, 75009

Dear Ms. Dupre,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PA21 (sucroferric oxyhydroxide) Chewable Tablets, 500 mg.

We also refer to your September 19, 2013 submission, containing updated labeling.

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

Office of Medication Error Prevention and Risk Management – Division of Medication Error Prevention and Analysis

A. General comments on all container labels and carton labeling

1. Revise the presentation of the proprietary name from all caps (i.e. VELPHORO) to title case (i.e. Velphoro) to improve readability of the name.
2. The proposed proprietary name “VELPHORO” is printed in two colors (“PHO” is blue in color and “VEL---RO” is black). This can be considered to be analogous to the use of tall-man lettering which is typically reserved for differentiating known look-alike and sound-alike established name pairs or in rare circumstances for proprietary names to help reduce the risk of wrong drug name errors² Since Velphoro is not a name that has been involved in drug name confusion or wrong drug errors, the use of different font colors in the name is inappropriately applied. Revise the proprietary name presentation so it is presented in a single font type and color.
3. Remove or minimize and move away the graphic near the proprietary name since it is distracting, competes with the prominence of the name, and may be mistaken as the letter ‘O’.
4. Ensure that the established name (including the dosage formulation) is at least half the size of the proprietary name. Ensure the established name has prominence commensurate with the proprietary name taking into account all pertinent factors including typography, layout, contrast and other printing features per 21 CFR 201.10(g)(2). The entire established name, including the active ingredient and the dosage form, should be presented in the same font.
5. Relocate the strength statement to appear below the established name statement on the principal display panel (PDP).

6. Debold the “Rx Only” statement and ensure the font size is smaller than the proprietary name, established name, and strength to minimize its prominence.

B. Blister Label

1. Remove the ‘Rx only’ statement to reduce clutter on the small label.
2. Debold and condense the distributor information to create more white space on this small label and improve readability.
3. The light grey color used for the NDC number is difficult to read. We recommend using a font color that will improve readability.

C. Container Label and Carton Labeling (30-count physician samples)

1. Increase the prominence of the statement “Physician Sample – Not For Sale” to avoid overlooking this important information.

D. Carton Labeling (30-count physician samples and 90-count bottles)

1. The back panel looks too similar to the principal display panel (PDP), which can lead to the wrong panel being displayed on a shelf during stocking. Revise the back panel to ensure adequate differentiation from the PDP.
2. Remove the proprietary name and established name printed vertically since it is not easily readable without having to turn or rotate the container and is redundant. Ensure the presentation of the proprietary name and established name on the principal display panel is prominently displayed, horizontally, in a manner congruent with the container labels.
3. Add the statement “Tablet must be chewed” on the principal display panel.
4. Relocate the net quantity statement from the back panel to the PDP. Ensure it is located away from the statement of strength.

E. Carton Labeling (30-count and 90-count unit-dose blisters)

1. Remove the proprietary name and established name in the blue portion of the principal display panel (PDP) and side panel since it is redundant.
2. Add the statement “Tablet must be chewed” on the PDP.

F. Carton Labeling (30-count unit-dose blisters)

1. Relocate the net quantity statement from the end panel to the principal display panel (PDP). Ensure it is located away from the statement of strength.

G. Bottle Container Label

1. Delete the words [REDACTED] ^{(b) (4)} from the “Tablets must be chewed...” statement and increase the prominence of the “Tablets must be chewed” statement.
2. Delete the [REDACTED] ^{(b) (4)} statement since it clutters the label and is not required.
3. The label is currently cluttered making it difficult to read the information being presented. Additionally, a reader will be required to turn the bottle to read the most important information. Therefore, we recommend rearranging the label into two sections: a principal display panel (PDP) and a side panel. The proprietary name, established name, strength, net quantity, and chewing warning should be retained on the PDP. Ensure the net quantity statement is located on the bottom of the PDP away from the strength statement while the “salt equivalent” statement is relocated to the side panel.

4. Delete the statement [REDACTED] (b) (4)
as it is repetitive and clutters the PDP. The asterisk may be relocated to follow the strength statement on the PDP.

If you have any questions, please call Anna Park, Regulatory Project Manager, at (301) 796-1129.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: Fresenius Medical Care North America
Attention: Ruth Turner
U.S. Agent for Vifor Fresenius Medical Care Renal Pharma
920 Winter Street
Waltham, MA 02451

21 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS)
immediately following this page.

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/s/

NORMAN L STOCKBRIDGE
10/10/2013

Bouie, Teshara

From: Bouie, Teshara
Sent: Thursday, September 26, 2013 1:04 PM
To: ruth.s.turner@fmc-na.com
Cc: Park, Anna
Subject: NDA 205109 - Information Request

Hi Ruth,

We have the following requests for information:

1. In your bottle and carton labels for the [REDACTED] (b) (4)
[REDACTED] Please clarify.

2. Make changes to all bottle container and carton labels and blister carton label as follows (see attached an example):

- Place an asterisk next to the 500 mg
- Take out the sentence [REDACTED] (b) (4)

[REDACTED] (b) (4)

Regards,

Teshara G. Bowie, MSA, OTR/L

CDR, United States Public Health Service
Regulatory Health Project Manager
FDA/CDER/OPS/ONDQA
Division of New Drug Quality Assessment I
Phone (301) 796-1649
Fax (301) 796-9749

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/s/

TESHARA G BOUIE
09/26/2013



NDA 205109

GENERAL ADVICE

Vifor Fresenius Medical Care Renal Pharma
Attention: Ms. Florence Dupre
President of VFMCRP France
12, Rue de la Chaussée d'Antin
Paris, France, 75009

Dear Ms. Dupre,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PA21 (sucroferric oxyhydroxide) Chewable Tablets, 500 mg.

We also refer to your September 3, 2013, amendment containing your revised pediatric study protocol, and your email dated September 6, 2013, requesting, in writing, the Division's comments/acceptance of the proposed changes in lieu of the face-to face meeting scheduled for September 12, 2013. The revised pediatric study protocol, PA-CL-PED-01, proposes "to remove Stage 1a (the fixed dose stage) and subjects would initiate study drug treatment in Stage 1 - a titration stage (formerly Stage 1b)." Doses of study drug may be increased or decreased as required for efficacy. Once a study participant achieves the age specific target serum phosphorus level, then the subject enters into Stage 2.

We have completed our review of your submission and have the following comments/recommendations:

Clinical

1. Concern for carry-over effect from previous phosphate binder usage: Please verify that there will be a 3 week wash-out period for those study participants who were taking phosphate binders prior to study entry.
2. Please consider the protocol recommendations provided in the preliminary comments, emailed to you on September 5, 2013.

If you have any questions, please call Anna Park, Regulatory Project Manager, at (301) 796-1129.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: Fresenius Medical Care North America
Attention: Ruth Turner
U.S. Agent for Vifor Fresenius Medical Care Renal Pharma

NDA 205109

Page 2

920 Winter Street
Waltham, MA 02451

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/s/

NORMAN L STOCKBRIDGE
09/25/2013

Bouie, Teshara

From: Bouie, Teshara
Sent: Thursday, September 19, 2013 1:18 PM
To: ruth.s.turner@fmc-na.com
Cc: Park, Anna
Subject: NDA 205109 - Information Request

Hi Ruth,

We have the following requests for information:

1. Amend your on-going stability protocol and post approval stability to add a 30 months time point to the on-going stability study protocol and the post-approval stability program at long-term (25°C/60% RH and 30°C/75% RH) storage conditions.
2. Provide tablet chewability information for tablets with hardness of (b) (4)

Please provide a response to this request no later than September 24, 2013.

Regards,

Teshara G. Bouie, MSA, OTR/L
CDR, United States Public Health Service
Regulatory Health Project Manager
FDA/CDER/OPS/ONDQA
Division of New Drug Quality Assessment I
Phone (301) 796-1649
Fax (301) 796-9749

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/s/

TESHARA G BOUIE
09/19/2013

Bouie, Teshara

From: Bouie, Teshara
Sent: Friday, September 06, 2013 10:44 AM
To: ruth.s.turner@fmc-na.com
Cc: Park, Anna
Subject: NDA 205109

Hi Ruth,

In reference to your response to question #9 dated July 31, 2013 for NDA 205109, we are in agreement with your proposal of expressing the Velphoro[®] chewable tablet as 500 mg iron. We recommend that the following equivalency statement be included on the drug product label.

Velphoro[®] (sucroferric oxyhydroxide) Chewable Tablet
500 mg*

* Each chewable tablet contains 500 mg elemental iron (equivalent to 2500 mg sucroferric oxyhydroxide complex).

We have the following additional questions:

- 1) In the event of accidental swallowing of the whole tablet or pieces of the tablets which may become lodged in esophagus, comment on the swelling and tissue (e.g. esophagus) adhesion properties of the tablets when in contact with an aqueous environment and in tissue contact.
- 2) Provide information on cases of accidental swallowing of whole tablets and any swallowing problems reported by the patients during clinical trials.

We request a response to this request before September 20, 2013.

Regards,

Teshara G. Bouie, MSA, OTR/L
CDR, United States Public Health Service
Regulatory Health Project Manager
FDA/CDER/OPS/ONDQA
Division of New Drug Quality Assessment I
Phone (301) 796-1649
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/s/

TESHARA G BOUIE
09/06/2013



NDA 205109

MEETING PRELIMINARY COMMENTS

Vifor Fresenius Medical Care Renal Pharma
Attention: Ms. Florence Dupre
President of VFMCRP France
12, Rue de la Chaussée d'Antin
Paris, France, 75009

Dear Ms. Dupre,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PA21 (sucroferric oxyhydroxide) Chewable Tablets, 500 mg.

Our preliminary responses to your meeting questions are enclosed.

You should provide, to the Regulatory Project Manager, a hardcopy or electronic version of any materials (i.e., slides or handouts) to be presented and/or discussed at the meeting.

If you have any questions, please call Anna Park, Regulatory Project Manager, at (301) 796-1129.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
Preliminary Meeting Comments



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

PRELIMINARY MEETING COMMENTS

Meeting Type: B

Meeting Date and Time: September 12, 2013
Meeting Location: 9:00 AM – 10:00 AM, EST

Application Number: NDA 205109
Product Name: PA21(sucroferric oxyhydroxide)
Indication: control of serum phosphorus levels in patients with end stage renal disease

Sponsor/Applicant Name: Vifor Fresenius Medical Care Renal Pharma France

FDA ATTENDEES (tentative)

Division of Cardiovascular and Renal Products

Norman Stockbridge, M.D., Ph.D.	Director
Shen Xiao, M.D., Ph.D.	Medical Officer
Martin Rose, M.D.	Medical Officer
Anna Park, R.Ph.	Regulatory Project Manager

Office of Clinical Pharmacology

Rajnikanth Madabushi, Ph.D.	Clinical Pharmacology and Biopharmaceutics Team Leader
Ju-Ping Lai, Ph.D.	Clinical Pharmacology Reviewer

Office of Biostatistics

Ququan (Cherry) Liu, M.D.	Statistician
---------------------------	--------------

Office of New Drug Assessment and Quality Assurance

Kasturi Srinivasachar, Ph.D.	Pharmaceutical Assessment Lead, Division of Premarketing Assessment I
Thomas Wong, Ph.D.	Product Quality Reviewer

Office of Pediatric and Maternal Health

Lynne P. Yao, M.D.	Associate Director, PMHS
Hari Cheryl Sachs, M.D.	Medical Team Leader, Pediatrics
Erica L. Wynn, M.D., M.P.H	Medical Officer
Lori Gorski	Regulatory Project Manager

SPONSOR ATTENDEES

Michael Bauer, Ph.D.	Director, Regulatory Affairs PA21
----------------------	-----------------------------------

Edward Chong, M.D.
Behruz Eslami, Ph.D.
Burkhard Kriwet, Ph.D.
Laura Lisk, BSc
Wolfgang Meder, Ph.D.
Patrick Moneuse, MSc
Stefan Wohlfeil, M.D.
Claude Miller
Claudy Mullon, Ph.D.
Ruth S. Turner
Jiao Wei, Ph.D.

Vice President, Head of Clinical Research
Senior Vice President, Global Regulatory Affairs
Vice President, Head of Technical Development
Director of Clinical Research
Director, Regulatory Affairs Team Leader PA21
Head of Biometrics
Senior Vice President, Chief Medical Officer
Vice President, Regulatory Affairs
Vice President, Clinical Research & Medical Affairs
Director, Regulatory Affairs
Principal Associate, Regulatory Affairs

Introduction:

This material consists of our preliminary responses to your questions and any additional comments in preparation for the discussion at the meeting scheduled for **September 12, 2013 from 9:00 AM – 10:00 AM, EST. in Bldg 22 Room 1309 between Vifor Fresenius Medical Care Renal Pharma France and the Division of Cardiovascular and Renal Products.** We are sharing this material to promote a collaborative and successful discussion at the meeting. The meeting minutes will reflect agreements, important issues, and any action items discussed during the meeting and may not be identical to these preliminary comments following substantive discussion at the meeting. However, if these answers and comments are clear to you and you determine that further discussion is not required, you have the option of cancelling the meeting (contact the regulatory project manager (RPM)). If you choose to cancel the meeting, this document will represent the official record of the meeting. If you determine that discussion is needed for only some of the original questions, you have the option of reducing the agenda and/or changing the format of the meeting (e.g., from face to face to teleconference). It is important to remember that some meetings, particularly milestone meetings, can be valuable even if the pre-meeting communications are considered sufficient to answer the questions. Note that if there are any major changes to your development plan, the purpose of the meeting, or the questions based on our preliminary responses, we may not be prepared to discuss or reach agreement on such changes at the meeting although we will try to do so if possible. If any modifications to the development plan or additional questions for which you would like CDER feedback arise before the meeting, contact the RPM to discuss the possibility of including these items for discussion at the meeting.

1.0 BACKGROUND

Vifor Fresenius Medical Care Renal Pharma (VFMCRP) has developed a new oral phosphate binder (PB), PA21, for therapeutic use in the control of serum phosphorus levels in patients with end-stage renal disease (ESRD). On February 1, 2013, with the new drug application (NDA) submission, the applicant requested a deferral of pediatric studies and was open to discuss an appropriate pediatric development plan after the safety and effectiveness of PA21 was established and the NDA was approved. (b) (4)



(b) (4)



2. DISCUSSION

2.1. Questions

1. Does the Agency concur with the use and choice of the active comparator in the proposed study?

FDA Response: Although there are no phosphate binders approved for pediatric use in the United States, calcium-based phosphate binders are recommended in current NKF KDOQI clinical practice guidelines as first line therapy in addition to dietary restrictions.

Based on the proposed safety monitoring procedures, dose adjustment, and stopping criteria, using Phoslyra (calcium-acetate) as the active comparator in this study is acceptable. However, as there is no established safety profile of Phoslyra in the pediatric population, you will need to document withdrawals, serious adverse events, and severe adverse events related to hypercalcemia and those adverse events that are commonly associated with calcium acetate in the adult study population. We recommend that if hypercalcemia develops in the control arm this should be counted as an adverse event and patients should either be withdrawn from the study, have the dose of the calcium based phosphate binder lowered, or be switched to a non-calcium containing phosphate binder. You should conduct a safety analysis of these events to determine if they occur more often in the Phoslyra group relative to the other control arm.

We note that, adequately powered, this study would provide information sufficient

(b) (4)



(b) (4)



4. Does the Agency concur that the study design as outlined in the synopsis is sufficient to support a pediatric indication for PA21? VFMCRP seeks Agency's concurrence on the following:
- Selection criteria, especially with the age-related serum phosphorus levels for inclusion in the study;
 - Primary efficacy end-points and primary efficacy analysis for PA21;
 - Sample size and duration of exposure;
 - Age groups and age-related dosing of study medications;
 - Age-related target serum phosphorus levels;
 - Safety monitoring procedures and safety endpoint
 - Palatability and acceptability patient reported outcomes (PRO) assessments

FDA Response: The (b) (4) will reflect the target population studied and the outcome results of data generated from the study

The study design is acceptable. The selection criteria, primary efficacy end-points, primary efficacy analysis for PA21, age-related target serum phosphorus levels, and safety monitoring procedures seem reasonable.

We have the following comments on your protocol:

- 1. Please provide additional rationale for your starting dose and how adult clinical data were used to determine the starting dose. In the absence of PK/PD data in pediatric patients, we recommend a staged approach in which dosing is initiated in an older age cohort, with sequential enrollment of younger age cohorts if data from older age cohort(s) suggest that efficacy can be achieved and there is no emergence of a safety signal.**
- 2. The small number of patients enrolled in the <1 year old age group are not adequate to provide meaningful safety or efficacy data. Therefore, we recommend that the proportion of patients in each of the four age groups be more similar. If you are unable to enroll a larger number of patients, you may have to provide additional support to justify partial extrapolation of your efficacy results from older pediatric patients to the younger age group.**
- 3. In order to account for any confounding that may result from dietary restrictions, all patients should have a food diary and dietary phosphorus restriction monitored.**

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/s/

NORMAN L STOCKBRIDGE
09/05/2013

From: Kovacs, Sarrit
To: [Xiao, Shen](#)
Cc: [Park, Anna](#); [Burke, Laurie B \(Laurie.Burke@fda.hhs.gov\)](#); [Papadopoulos, Elektra \(Elektra.Papadopoulos@fda.hhs.gov\)](#); [Slagle, Ashley \(Ashley.Slagle@fda.hhs.gov\)](#); [CDER SEALD Endpoints](#)
Subject: SEALD's response to DCRP's consult request (NDA 205109)
Date: Tuesday, August 13, 2013 3:55:00 PM

Dear Dr. Xiao,

This email is in response to a SEALD consult request made by DCRP to evaluate the PRO instruments assessing palatability and acceptability that Fresenius Medical Care is proposing to include in an upcoming pediatric study (NDA 205109). Please be advised that SEALD only reviews the methodological adequacy of primary and key secondary endpoints (i.e., those that have appropriate multiplicity adjustment in the statistical analysis plan) [REDACTED] (b) (4). A SEALD endpoint review is not necessary for exploratory endpoints [REDACTED] (b) (4).

Upon review of the instruments, PRO evidence dossier, and briefing document, [REDACTED] (b) (4) [REDACTED] using these instruments for exploratory purposes. Although the sponsor refers to the PRO instruments as a secondary endpoint, these instruments are not being scored (only descriptive statistics will be used) and they are being treated as an exploratory endpoint. This becomes clear in Section VII ("Interpretation of Scores") on page 4 of the PRO evidence dossier. In addition, there are no specific questions from the sponsor [REDACTED] (b) (4) [REDACTED].

Therefore, SEALD does not intend to provide a written review or attend the upcoming meetings for this consult. SEALD will file this email response in DARRTS to close out this consult request.

Please let us know if you have any questions.

Thank you,
Sarrit

Sarrit M. Kovacs, Ph.D.
Study Endpoints Reviewer (SEALD)

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/s/

SARRIT M KOVACS
08/13/2013

ELEKTRA J PAPADOPOULOS
08/13/2013

LAURIE B BURKE
08/13/2013



NDA 205109

INFORMATION REQUEST

Vifor Fresenius Medical Care Renal Pharma France
c/o Fresenius Medical Care North America (FMCNA)
Attention: Ruth Turner, US Agent
920 Winter Street
Waltham, MA 02451

Dear Ms. Turner:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [REDACTED] (b) (4) Tablets.

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

Drug substance:

1. Since the active moiety is iron(III)-oxyhydroxide, apply for a USAN name for this active moiety. Inform us once the USAN name is available.
2. S.2.2 – Description of Manufacturing Process and Process Controls.

Provide process parameters such as [REDACTED] (b) (4)

3. S.2.3 - Control of materials:

According to most recent published Provisional Tolerable Weekly Intake (PTWI) from The Joint FAO/WHO Expert Committee on Food Additives (JECFA) and European Food Safety Authority, the limit for [REDACTED] (b) (4) Your proposed acceptance limit for [REDACTED] (b) (4)

4. S.2.4 - Control of critical steps:

Provide data to support your proposed in-process control limits for [REDACTED] (b) (4)

5. S.4.1 - Drug substance specification:

- a. In the drug substance specification include a test with acceptance criteria for (b) (4) stated in the pre-NDA CMC meeting on 7 December 2012.
- b. Designate one of the test methods for the LOD, assays, and in-vitro phosphate adsorption as the regulatory method and the other as an alternate method. In addition, it is mentioned that in Method 2 for in-vitro phosphate adsorption, either ICP-OES or UV/VIS method can be used to measure the content of phosphate. For Method 2, one of the detection methods for the phosphate content should also be chosen as the regulatory method and the other as an alternate method.
- c. The regulatory method for the ID test should be NIR.
- d. Remove Footnotes 3 – 8 and the Notes and consolidate compendial references in the Method Reference column, e.g USP/Ph. Eur.

6. S.4.5 – Justification of specification:

The justification of the particle size distribution limit was based on the tablet manufacturing experience. In Section 3.2.P.2.1.1.1 Influence of Particle Size, it was mentioned that the effect of the particle size distribution of the drug substance on the phosphate adsorption was evaluated during formulation development. Justify the acceptance limit for the particle size at (b) (4) based on the results of phosphate adsorption study.

Drug product:

7. P.3.3.2 - Detailed description for the method of manufacture:

(b) (4)

8. P.5.1 - Drug product specification:

- a. The test for iron release should be included in the specification and performed both at batch release and stability.
- b. Designate one of the test methods for the LOD, assays and in-vitro phosphate as regulatory method and the other as an alternate method. In addition, it is mentioned that in Method 2 for in-vitro phosphate adsorption, either ICP-OES or UV/VIS method can be used to measure the content of phosphate. For Method 2, one of the detection methods for the phosphate content should also be chosen as the regulatory method and the other as an alternate method.
- c. The regulatory method for the ID test should be NIR.
- d. Remove footnotes 3 – 8 and the Notes and consolidate compendial references in the Method Reference column.
- e. Periodic testing for microbiological quality is not acceptable. This test should be performed on each batch at release and stability.

9. The labeling strength of the chewable tablet should be:

Trade name (established name of active moiety, e.g., polynuclear iron (III)-oxyhydroxide) chewable tablet, (b) (4)

*equivalent to 500 mg iron.

Biopharmaceutics:

10. Revise the agitation speed of your proposed dissolution method (b) (4) 50 rpm, and provide appropriate updates to section P.5.1 and P.5.2 of your NDA.
11. Provide dissolution profile data using 50 rpm (individual, mean, SD, tables and figure) for your clinical (156001A11, 014011B11, 014011C11) and stability/ registration batches.
12. Provide comparative dissolution profile data using 50 rpm (individual, mean, SD, tables and figure), including f2 testing, for drug product batches (b) (4)
13. Provide comparative dissolution profile data using 50 rpm (individual, mean, SD, tables and figure), including f2 testing, for drug product batches containing PA21-1 and PA21-2.
14. Provide comparative dissolution profile data using 50 rpm (individual, mean, SD, tables and figure), for drug product batches with different tablet hardness (b) (4)

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

Sincerely,

{See appended electronic signature page}

Ramesh Sood, Ph.D.
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/

RAMESH K SOOD
07/11/2013



NDA 205109

GENERAL ADVICE

Vifor Fresenius Medical Care Renal Pharma
Attention: Ms. Florence Dupre
President of VFMCRP France
12, Rue de la Chaussée d'Antin
Paris, France, 75009

Dear Ms. Dupre,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PA21 (b)(4) Chewable Tablets, 500 mg.

Our review of your NDA application are still ongoing, however, we have identified the following review issues:

Pharmacology

In the label Section 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility, you states that (b)(4)

Treatment-related neoplastic adenocarcinomas were seen in mouse colon and cecum with all (b)(4) dose groups. There were also (b)(4) dose-related increases in incidence and/or severity of GI epithelial hyperplasia in mice and increased incidence of GI epithelial/mucosal hyperplasia in (b)(4)-treated rats. Although the dog was negative for GI changes, this may be because of the reduced residence time resulting from chronic diarrhea seen in these animals.

As you know, chronic GI irritation, inflammation, and./or hyperplasia are known risk factors for development of GI cancer in humans. (b)(4)

(b)(4) you will need to demonstrate absence of GI epithelial/mucosal hyperplasia in a second large animal species, such as the monkey, treated chronically (e.g., 13 weeks) with (b)(4) Otherwise, (b)(4) rodent findings because of its relevance for humans treated chronically with (b)(4)

Clinical

1. Please clarify how the data of “discolored feces” were collected. Is it based on the patient’s report or the investigator’s examination? If the iron is the reason of the discolor feces, then we do not understand the significant reduction of its incidence rate in the long-term study compared to the first 4 weeks study in the Study PA-CL-05A.

2. The incidence rate of diarrhea was significantly different between the Study PA-CL-03A and 05A compared to Sevelamer. To what do you attribute this difference?
3. In general, oral iron supplements should not interfere with the fecal occult blood test. Please confirm if the PA21 is similar to other iron supplements as the dosage of iron in PA21 is much higher than the regular iron supplements.

If you have any questions, please call Anna Park, Regulatory Project Manager, at (301) 796-1129.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: Fresenius Medical Care North America
Attention: Ruth Turner
U.S. Agent for Vifor Fresenius Medical Care Renal Pharma
920 Winter Street
Waltham, MA 02451

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/s/

NORMAN L STOCKBRIDGE
07/05/2013

REQUEST FOR Patient Reported Outcomes (PRO) ENDPOINTS CONSULTATION

TO: Study Endpoints and Labeling Development (SEALD) CDER/OND-IO White Oak Bldg 22, Mail Drop 6411 SEALD.ENDPOINTS@FDA.HHS.GOV		FROM: Review Division: DCRP Medical Reviewer: Shen Xiao Project Manager: Anna Park		
DATE OF CONSULT REQUEST June 25, 2013	Application# NDA 205109	LETTER # OR SUBMISSION # SDN# 16 (DARRTS)	TYPE OF DOCUMENT (Meeting; Protocol/SPA; PDUFA Product Review) Meeting	REQUESTED SEALD COMPLETION DATE* August 27, 2013
DRUG ESTABLISHED NAME PA21 chewable tablet, 500 mg	DRUG TRADE NAME Velphoro	NAME OF SPONSOR Fresenius Medical Care	SPONSOR SUBMIT DATE June 25, 2013	

DEVELOPMENT PHASE: NDA
GOAL DATE (if NDA/BLA./SPA): December 1, 2013
ELECTRONIC LINK (if applicable): EDR Location: [\CDSESUB1\EVSPROD\NDA205109\0015](#)
BACKGROUND PACKAGE (deliver PAPER to CDER SEALD Endpoints mailbox in Bldg 22, Rm 6411):
MEETINGS (if applicable) (please send invite to SEALD.ENDPOINTS@FDA.HHS.GOV)
 Meeting type (A, B, C): C

 Internal Meeting date: 08/28/13
 Sponsor/Industry Meeting date: 9/12/13

PLEASE make certain the background-briefing package is included with this consult. It should contain the following applicable information needed to start Study Endpoints Review: Protocol or Study ID; Endpoint Concept(s); Instrument(s); Indication(s); Study population(s); Prior related reviews. Division PM, please provide the following specific information on this consult form:

Instrument(s): Assessment of Palatability and Acceptability

Indication(s): phosphate binder

Specific Questions/Comments for SEALD: Please help to determine if the proposed PRO protocol is valid for evaluating the acceptability and palatability of this product in the pediatric study. If possible, the sponsor would appreciate feedback on their protocol.

Requester: Anna Park

Name/Phone number/email address/office location

61129; anna.park@fda.hhs.gov; bldg. 22 Room 4156

Glossary:

Concept: The specific goal of a measurement (i.e. the *thing* that is to be measured by a PRO instrument).

Instrument: A means to capture data (e.g. questionnaire, diary) plus all the information and documentation that supports its use. Generally, that includes clearly defined methods and instructions for administration or responding, a standard format for data collection, and well-documented methods for scoring, analysis, and interpretation of results.

*For voluminous study endpoint submissions (e.g. PRO “dossier” or content validity documentation greater than 50 pages), SEALD requests 60 days after receiving the background/briefing package document to complete the review.

PA21 Paediatric Protocol (PA-CL-PED-01) - Assessment of Palatability and Acceptability: Patient Reported Outcomes (PROs) Under Consideration

The current Patient Reported Outcomes (PROs) being considered for collection of palatability/acceptability data on study drugs in the above study are as follows:

Subjects >2 years to <18 years

For subjects >2 years to ≤6 years of age an 'assisted' mode will be used i.e. the parent/carer will mark the form on behalf of the child, in discussion with them.

1. Overall like/dislike of the study drugs will be assessed using a 5-point Hedonic scale:



- a. >2 years to ≤ 6 years: just faces.
 - b. > 6 years: faces and words.
-
2. Visual Analogue Scales (VAS) will be used to assess:
 - a. Compliance with the study drug compared with other phosphate binders.
 - b. Overall ease of taking/administering the study drug.
 - c. Palatability/acceptability of the study drug compared with other medications the subject has to take.

Subjects ≤ 2 years

For subjects ≤ 2 years PROs will be administered by the parent/carer using a simplified response form directly tailored to them:

1. Did you experience any difficulty giving this medicine to your child? Yes/No.
2. If you answered "Yes" to the 1st question please explain why you gave that answer?
3. Did it appear to you that your child found the medicine more acceptable or less acceptable than other medications they have to take? More acceptable/Less acceptable.

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/s/

ANNA J PARK
06/25/2013



NDA 205109

MEETING REQUEST GRANTED

Vifor Fresenius Medical Care Renal Pharma
Attention: Ms. Florence Dupre
President of VFMCRP France
12, Rue de la Chaussée d'Antin
Paris, France, 75009

Dear Ms. Dupre,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PA21 [REDACTED] ^{(b) (4)} Chewable Tablets, 500 mg.

We also refer to your June 17, 2013 correspondence requesting a meeting to discuss your pediatric formulation and pediatric study outline.

The meeting is scheduled as follows:

Date: September 12, 2013
Time: 9:00 AM – 10:00 PM, EST
Location: 10903 New Hampshire Avenue
White Oak Building 22, Conference Room: 1309
Silver Spring, Maryland 20903

Invited CDER Participants:

Division of Cardiovascular and Renal Products

Norman Stockbridge, M.D., Ph.D.	Director
Aliza Thompson, M.D.	Medical Team Leader
Shen Xiao, M.D.	Medical Officer
Thomas Papoian, Ph.D.	Pharmacology Team Leader
Xavier Joseph, Ph.D.	Pharmacology Reviewer
Anna Park, R.Ph., RAC	Regulatory Project Manager

Office of Clinical Pharmacology

Rajnikanth Madabushi, Ph.D.	Clinical Pharmacology and Biopharmaceutics Team Leader
Ju-Ping Lai, Ph.D.	Clinical Pharmacology Reviewer

Office of Biostatistics

James Hung, Ph.D.

Director, Division of Biometrics I, Office of
Biostatistics (OB)

Ququan (Cherry) Liu, M.D.

Statistician

Office of New Drug Assessment and Quality Assurance

Kasturi Srinivasachar, Ph.D.

Pharmaceutical Assessment Lead, Division of
Premarketing Assessment I

Thomas Wong, Ph.D.

Product Quality Reviewer

Elsbeth Chickhale, Ph.D.

Biopharmaceutics Reviewer

Pediatric and Maternal Health Staff

Hari Sachs, M.D.

Medical Team Leader

Erica L. Wynn, M.D.

Medical Officer

Lori Gorski

Regulatory Project Manager

Please e-mail me any updates to your attendees at anna.park@fda.hhs.gov, at least one week prior to the meeting. For each foreign visitor, complete and email me the enclosed Foreign Visitor Data Request Form, at least two weeks prior to the meeting. A foreign visitor is any non-U.S. citizen who does not have Permanent Resident Status or a valid U.S. Federal Government Agency issued Security Identification Access Badge. If we do not receive the above requested information in a timely manner, attendees may be denied access.

A few days before the meeting, you may receive an email with a barcode generated by FDA's Lobbyguard system. If you receive this email, bring it with you to expedite your group's admission to the building. Ensure that the barcode is printed at 100% resolution to avoid potential barcode reading errors.

Please have all attendees bring valid photo identification and allow 15-30 minutes to complete security clearance. Upon arrival at FDA, provide the guards with the following numbers to request an escort to the conference room: Anna Park at (301)796-1129.

Submit background information for the meeting (three paper copies or one electronic copy to the application and 23 desk copies to me) at least four weeks prior to the meeting. If the materials presented in the information package are inadequate to prepare for the meeting or if we do not receive the package by August 15, 2013, we may cancel or reschedule the meeting.

Submit the 23 desk copies to the following address:

LCDR Anna Park
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 4156

10903 New Hampshire Avenue
Silver Spring, Maryland

*Use zip code **20903** if shipping via United States Postal Service (USPS).*

*Use zip code **20993** if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

If you have any questions, please call me at (301) 796-1129.

Sincerely,

{See appended electronic signature page}

LCDR Anna Park, R.Ph., RAC
Senior Regulatory Management Officer
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure:
Foreign Visitor Data Request Form

cc: Fresenius Medical Care North America
Attention: Ruth Turner
U.S. Agent for Vifor Fresenius Medical Care Renal Pharma
920 Winter Street
Waltham, MA 02451

FOREIGN VISITOR DATA REQUEST FORM

VISITORS FULL NAME (First, Middle, Last)	
GENDER	
COUNTRY OF ORIGIN/CITZENSHIP	
DATE OF BIRTH (MM/DD/YYYY)	
PLACE OF BIRTH (city and country)	
PASSPORT NUMBER COUNTRY THAT ISSUED PASSPORT ISSUANCE DATE: EXPIRATION DATE:	
VISITOR ORGANIZATION/EMPLOYER	
MEETING START DATE AND TIME	September 12, 2013 09:00 AM, EST
MEETING ENDING DATE AND TIME	September 12, 2013 10:00 PM, EST
PURPOSE OF MEETING	Discuss pediatric plan
BUILDING(S) & ROOM NUMBER(S) TO BE VISITED	Bldg 22 Room 1309
WILL CRITICAL INFRASTRUCTURE AND/OR FDA LABORATORIES BE VISITED?	no
HOSTING OFFICIAL (name, title, office/bldg, room number, and phone number)	LCDR Anna Park, R.Ph., RAC Bldg 22 Room 4156 (301)796-1129
ESCORT INFORMATION (If different from Hosting Official)	

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/s/

ANNA J PARK
06/20/2013



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 205109

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Vifor Fresenius Medical Care Renal Pharma France
c/o: Fresenius Medical Care North America (FMCNA)
920 Winter Street
Waltham, MA 02451

ATTENTION: Ruth Turner
Director, Regulatory Affairs Pharmaceuticals
US Agent

Dear Ms. Turner:

Please refer to your New Drug Application (NDA) dated January 31, 2013, received February 1, 2013, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for PA21 Chewable Tablets, 500 mg.

We also refer to your March 13, 2013, correspondence, received March 13, 2013, requesting review of your proposed proprietary name, Velphoro. We have completed our review of the proposed proprietary name and have concluded that it is acceptable.

The proposed proprietary name, Velphoro, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you. If **any** of the proposed product characteristics as stated in your March 13, 2013, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Cheryle Milburn, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-2084. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Michael Monteleone, at (301) 796-1952.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

CAROL A HOLQUIST
06/10/2013



NDA 205109

FILING COMMUNICATION

Vifor Fresenius Medical Care Renal Pharma
Attention: Ms. Florence Dupre
President of VFMCRP France
12, Rue de la Chaussée d'Antin
Paris, France, 75009

Dear Ms. Dupre,

Please refer to your New Drug Application (NDA) dated January 31, 2013, received February 1, 2013 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PA21
[REDACTED] ^{(b) (4)} Chewable Tablets, 500 mg.

We also refer to your amendments dated February 15, 17, 18, March 8, 11, 13, 15, 28, and April 3, 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 1, 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 1, 2013.

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

- 1. Highlights (HL):**
 - a. All contraindications listed in the FPI must also be listed in HL or must include the statement “None” if no contraindications are known**
- 2. Full Prescribing Information (FPI):**

- a. **The following heading must appear at the beginning of the FPI in UPPER CASE and bolded: “FULL PRESCRIBING INFORMATION”**
 - b. **The bolded section and subsection headings must be named and numbered in accordance with 21 CFR 201.56(d)(1). Section 13.2 should be named “Animal Toxicity and/or Pharmacology”**
- 3. FULL PRESCRIBING INFORMATION DETAILS**
- a. **If no Contraindications are known, this section must state “None”.**

We request that you resubmit labeling that addresses these issues by **April 23, 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.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

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

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

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

REQUIRED PEDIATRIC ASSESSMENTS

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

We acknowledge receipt of your February 1, 2013 request for a full deferral of pediatric studies for this application. (b) (4)

If you have any questions, please call Anna Park, Regulatory Project Manager, at (301) 796-1129.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: Fresenius Medical Care North America
Attention: Ruth Turner
U.S. Agent for Vifor Fresenius Medical Care Renal Pharma
920 Winter Street
Waltham, MA 02451

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/s/

NORMAN L STOCKBRIDGE
04/09/2013

Executive CAC

Date of Meeting: April 2, 2013

Committee: David Jacobson-Kram, Ph.D., OND IO, Chair
Abby Jacobs, Ph.D., OND IO, Member
Paul Brown, Ph.D., OND IO, Member
Karen Davis Bruno, Ph.D., DMEP, Alternate Member
Thomas Papoian, Ph.D., DABT, DCRP, Team Leader
Baichun Yang, Ph.D., DABT, DCRP, Presenting Reviewer

Author of Draft: Baichun Yang

The following information reflects a brief summary of the Committee discussion and its recommendations.

NDA 205109

Drug Name: [REDACTED] ^{(b) (4)} (drug code: PA21; iron content 20%)

Sponsor: Vifor Fresenius Medical Care Renal Pharma; France

Background:

The new drug application (NDA) package for [REDACTED] ^{(b) (4)} (PA21, an insoluble phosphate binder) has been submitted to the Agency. The applicant is seeking marketing approval for the drug as a treatment for the “control of serum phosphorus levels in patients with end-stage renal disease (ESRD)”. The proposed regimen starts with chewing one 2500-mg tablet (500 mg iron) 3 times daily with meals and is adjusted by 1 tablet per day as needed until an acceptable serum phosphorus level (≤ 5.5 mg/dL) is reached, with a maximal daily dose of 6 tablets (3000 mg iron). The applicant has conducted two-year carcinogenicity studies in mice and rats.

Rat Carcinogenicity Study

PA21 carcinogenicity in Sprague Dawley rats was assessed at doses of 0, 200, 750, and 2500 mg/kg/day in the diet (iron dose = 0, 40, 150, and 500 mg/kg/day, respectively). Dose selection was based on an MTD as follows: 33% and 19% reduction in body weight gain in males and females, respectively, and one possible treatment-related death at 3000 mg/kg/day in a 13-week study.

The survival rate across the dose groups in the carcinogenicity study was similar to control. There were PA21-related alterations in urine/plasma phosphorus and calcium levels and increased bone turnover, indicating that the PA21 dose was high enough to cause toxicity in rats. Epithelial hyperplasia was observed in intestines at the high dose (Table 1). No drug-related neoplasms were observed in rats. Systemic exposure was not assessed since PA21 is practically insoluble and already known to be not absorbed.

Mouse Carcinogenicity Study

PA21 carcinogenicity in CD-1 mice was assessed at doses of 0, 1250, 2500, 5000 mg/kg/day in the diet (iron dose = 0, 250, 500, and 1000 mg/kg/day, respectively). The Exec CAC previously concurred with selection of the high dose using an MTD based on impaired renal function and urinary calculi.

The survival rate across the dose groups in the carcinogenicity study was similar to control. Colon and/or cecum adenocarcinomas were seen in all male treatment groups and in females at the high dose group with a single incidence in a female at the low dose group (Table 1). There were dose-related increases in incidences and severity of colon and/or cecum epithelial hyperplasia and mucosal diverticuli/cysts/hyperplasia, and epithelial hyperplasia and hyperkeratosis in the non-glandular portion of forestomach at the high dose (Table 1). Systemic exposure was not assessed since PA21 is practically insoluble and already known to be not absorbed.

Table 1. Proliferative (neoplastic and non-neoplastic) findings in gastrointestinal tract of all animals in the 2-year studies

Species	Organ	Findings	Male				Female			
			Control	Low	Mid	High	Control	Low	Mid	High
Rat	<i>Number of animal examined</i>		56-60	59-62	57-63	59-63	62-64	62-64	63-65	65
	Duodenum	Epithelial Hyperplasia	5	2	2	5	3	6	6	10
	Cecum	Epithelial Hyperplasia	1	0	2	9	0	0	0	8
	Colon	Epithelial Hyperplasia	0	0	1	6	0	0	0	8
		Submucosal Inflammation	1	0	0	4	1	0	1	7
Mouse	Cecum	<i>Number of animal examined</i>	51	58	50	54	57	54	55	59
		Adenocarcinoma	0	1	2	1	0	1	0	0
		Adenoma	0	0	0	1	0	0	0	0
		Epithelial Hyperplasia	2	3	3	15	0	0	0	8
		Mucosal Diverticulum/ Cysts/Epithelial Hyperplasia	0	3	4	12	0	0	0	3
	Colon	<i>Number of animal examined</i>	57	60	57	60	59	58	57	60
		Adenocarcinoma[#]	1	3	5	9**	0	0	0	3
		Epithelial Hyperplasia	5	16	22	25	3	5	6	21
	Stomach, Nonglandular region	<i>Number of animal examined</i>	58	60	60	60	60	59	59	60
		Epithelium Hyperplasia	3	1	3	9	0	0	2	3
		Hyperkeratosis	3	1	5	12	1	4	4	5

Dose level: Low=200, Mid=75, and High=2500 mg/kg/day in rats; Low=1250, Mid=2500, and High=5000 mg/kg/day in mice. # Dose response for colon adenocarcinoma, p=0.0012 in males and p=0.0164 in females.

** p<0.01 vs control.

Executive CAC Recommendations and Conclusions:

Rat:

- The Committee found that the study was acceptable.
- The Committee concurred that there were no drug-related neoplasms.

Mouse:

- The Committee found that the study was acceptable, noting prior Exec CAC concurrence with the protocol.
- The Committee concurred that the colon and/or cecum adenocarcinomas in all male treatment groups were clearly drug-related and noted a numerical increase in the incidence of colon adenocarcinomas in high dose females that did not reach statistical significance, but which was accompanied by dosed-related hyperplasia in the colon.

David Jacobson-Kram, Ph.D.
Chair, Executive CAC

cc:\n
/NDA 205109, DCRP
/Thomas Papoian, DCRP
/Baichun Yang, DCRP
/Anna Park, DCRP
/Adele Seifried, OND IO

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/s/

ADELE S SEIFRIED
04/03/2013

DAVID JACOBSON KRAM
04/03/2013



NDA 205109

GENERAL ADVICE

Vifor Fresenius Medical Care Renal Pharma
Attention: Ms. Florence Dupre
President of VFMCRP France
12, Rue de la Chaussee d'Antin
Paris, France, 75009

Dear Ms. Dupre,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PA21 [REDACTED] (b) (4) Chewable Tablets, 500 mg.

We also refer to your March 11, 2013 submission, containing your response to our February 13, 2013 Advice Letter in which the Agency concluded that PA21 [REDACTED] (b) (4) [REDACTED] was not a new molecular entity (NME) and would not be reviewed under the Program.

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

The active moiety in PA 21 is [REDACTED] (b) (4) which is the same active in currently marketed therapies for treatment of iron deficiency and anemia e.g. Venofer. This fact precludes PA 21 from being a New Molecular Entity. It is acknowledged that the polynuclear ferric oxyhydroxide core has been manipulated by stabilization, complexation etc. with carbohydrates depending on the indication sought, phosphate binding or systemic iron absorption. However, these modifications, though essential for the desired therapeutic indication, do not alter the fact that the active, [REDACTED] (b) (4) has been approved by FDA in other applications submitted under section 505(b) of the act.

If you have any questions, please call Anna Park, Regulatory Project Manager, at (301) 796-1129.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: Fresenius Medical Care North America
Attention: Ruth Turner
U.S. Agent for Vifor Fresenius Medical Care Renal Pharma
920 Winter Street
Waltham, MA 02451

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/s/

NORMAN L STOCKBRIDGE
04/03/2013



NDA 205109

INFORMATION REQUEST

Vifor Fresenius Medical Care Renal Pharma France
c/o Fresenius Medical Care North America (FMCNA)
Attention: Ruth Turner, US Agent
920 Winter Street
Waltham, MA 02451

Dear Ms. Turner:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [REDACTED] (b) (4) Tablets.

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

As discussed previously during the Pre-NDA meeting on December 7, 2012, your proposal [REDACTED] (b) (4) instead of dissolution as a quality control test in the drug product specifications is not acceptable. To continue the dissolution method development for your product, we recommend that you test additional paddle speeds (50 rpm [REDACTED] (b) (4)) and evaluate if [REDACTED] (b) (4) is appropriate for your product.

1. Submit a revised dissolution method development report with the updated information. The dissolution method development report should include the following:
 - a. Solubility data for the drug substance covering the pH range;
 - b. Detailed description of the dissolution test being proposed for the evaluation of your proposed drug product and the developmental parameters used to select the proposed dissolution method as the optimal test for the proposed product (*i.e.*, *selection of the equipment/ apparatus, in vitro dissolution media, agitation/rotation speed, pH, assay, sink conditions, etc.*). Include the data supporting the selection of the type and amount of surfactant. The testing conditions used for each test should be clearly specified. The dissolution profile should be complete (*i.e.*, 15, 20, 30, 45, & 60 minutes) and cover at least [REDACTED] (b) (4) of drug release of the label amount or whenever a plateau (*i.e.*, no increase over 3 consecutive time-points) is reached. We recommend that at least twelve samples be used per testing variable;

- c. Provide the complete dissolution profile data (*individual, mean, SD, profiles*). The dissolution data should be reported as the cumulative percentage of drug dissolved with time (*the percentage is based on the product's label claim*); and
- d. Include the complete dissolution data for the testing conducted to demonstrate the discriminating capability of the selected dissolution test as well as the supportive validation data for the dissolution method (i.e., method robustness, etc.) and analytical method (precision, accuracy, linearity, stability, etc.).

For the setting of the dissolution acceptance criteria of your product, the following points should be considered:

- e. The dissolution profile data (*i.e., 15, 20, 30, 45, & 60 minutes*) from the clinical batches and primary (registration) stability batches should be used for the setting of the dissolution acceptance criteria of your proposed drug product.
 - f. The *in vitro* dissolution profile should encompass the timeframe over which at least (b) (4) of the drug is dissolved or where the plateau of drug dissolved is reached, if incomplete dissolution is occurring.
 - g. The selection of the specification time point should be where $Q =$ (b) (4) dissolution occurs. However, if you have a slowly dissolving product or includes a BCS-Class 2, poor-soluble drug, a two-point specifications option may be adequate for your product. The first time point should be during the initial dissolution phase (i.e., 15-20 minutes) and the second time point should be where $Q =$ (b) (4) dissolution occurs.
 - h. The dissolution acceptance criterion should be based on average dissolution data (n=12).
2. The dissolution data that you collect during your stability study should cover the complete dissolution profile (*i.e., 15, 20, 30, 45, & 60 minutes*). Please provide these data. If you have not collected these dissolution data at all appropriate time points, you should start collecting these data and submit to the NDA.

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

Sincerely,

{See appended electronic signature page}

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

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/s/

RAMESH K SOOD
03/20/2013

OSI/DGCPC CONSULT: Request for Clinical Inspections

Date: March 19, 2013

To: Ann Meeker-O'Connell, Acting Division Director, DGPCPC
Constance Lewin, M.D., M.P.H, Branch Chief, GCPEB*
Susan Thompson, M.D., Acting Branch Chief, GCPAB
Janice Pohlman, M.D., M.P.H., Team Leader GCPAB
Susan Leibenhaut, M.D. Acting Team Leader, GCPAB
CDER OSI PM Track
Sharon Gershon, Pharm.D.
Division of Good Clinical Practice Compliance
Office of Scientific Investigations
Office of Compliance/CDER

Through: Shen Xiao, M.D., Cross-Discipline Team Leader and Clinical Reviewer, Division of Cardiovascular and Renal Products (DCRP)
Norman Stockbridge, M.D., Ph.D. Division Director (DCRP)

From: Anna Park, R.Ph., RAC Regulatory Health Project Manager/DCRP

Subject: Request for Clinical Site Inspections

I. General Information

Application#: NDA 205109
Applicant/ Applicant contact information (to include phone/email):
Vifor Fresenius Medical Care Renal Pharma France
Attention: Ms. Florence Dupre
President of VFMCRP France
12, Rue de la Chaussee d'Antin
Paris, France, 75009 Phone: +33 1 80 04 16 34

US Agent: Fresenius Medical Care North America (FMCNA)
Attention: Ruth Turner, Director, Regulatory Affairs – Pharma Email: Ruth.S.Turner@fmc-na.com
920 Winter Street Waltham, MA 02451 Phone: (781) 699-4654
Drug Proprietary Name: Velphoro
Generic Drug Name: PA21 (b) (4)
NME or Original BLA (Yes/No/Not Applicable*): TBD
Review Priority (Standard or Priority or Not Applicable*): Standard

Study Population includes < 17 years of age (Yes/No): No
Is this for Pediatric Exclusivity (Yes/No/Not Applicable*): No

OSI/DGCPC Consult
version: 01/16/2013

**For inspection requests not connected to a PDUFA timeline (i.e., for-cause when marketing application is not pending for product)*

Proposed New Indication(s): Control of serum phosphorus levels in patients with end stage renal disease (ESRD).

PDUFA: TBD

Action Goal Date: November 30, 2013

Inspection Summary Goal Date:

II. Protocol/Site Identification

Include the Protocol Title or Protocol Number for all protocols to be audited. Complete the following table (Note: ALL items listed are required, to process inspection request. Failure to provide complete information will result in delay of inspection process).

Site # (Name,Address, Phone number, email, fax#)	Protocol ID	Number of Subjects	Indication/Primary endpoint and other endpoints for verification
<p style="text-align: center; color: red;">#832</p> <p>USA Dr. Robert Hootkins Research Management, Inc. 12221 N. Mopac Expressway Austin, TX 78758 Tel: <u>(512) 284-1445</u> Fax: <u>(866) 910-0971</u> <u>rhootkins@researchmanagement.org</u></p>	<p>VIFOR PA-CL-05A</p>	<p>21</p>	<p>Indication: The control of serum phosphorus levels in patients with end-stage renal disease (ESRD).</p> <p>Primary efficacy endpoint: Change from Week 24, D1 in serum phosphorus levels at Week 27, D1 – a superiority comparison between the PA21 MD group and the PA21 LD control group (fixed dose of 1.25 g/day) in the primary efficacy set (PES) of subjects on HD (D1 refers to the first dialysis session of the week).</p>

Site # (Name,Address, Phone number, email, fax#)	Protocol ID	Number of Subjects	Indication/Primary endpoint and other endpoints for verification
<p style="text-align: center; color: red;">#833</p> <p>USA Dr. Susan Adele Diamond San Antonio Kidney Disease Center Physicians Group PLLC 8042 Wurzbach Road, Suite 500 San Antonio, TX 78229 Tel: <u>(210) 692.7864</u> Fax: <u>(210) 481.5159</u> <u>sdiamond@sakdc.com</u></p>	<p>VIFOR PA-CL-05A</p>	<p>22</p>	<p>Indication: The control of serum phosphorus levels in patients with end-stage renal disease (ESRD).</p> <p>Primary efficacy endpoint: Change from Week 24, D1 in serum phosphorus levels at Week 27, D1 – a superiority comparison between the PA21 MD group and the PA21 LD control group (fixed dose of 1.25 g/day) in the primary efficacy set (PES) of subjects on HD (D1 refers to the first dialysis session of the week).</p>
<p style="text-align: center; color: red;">#841</p> <p>USA Dr. A. Kaldun Nossuli Kaldun Nossuli, MD, PA 6420 Rockledge Drive Suite 1100 Bethesda, MD 20814 Tel: <u>(301) 907-4646</u> Fax: <u>(301) 907-7796</u> <u>knossuli@msn.com</u></p>	<p>VIFOR PA-CL-05A</p>	<p>15</p>	<p>Indication: The control of serum phosphorus levels in patients with end-stage renal disease (ESRD).</p> <p>Primary efficacy endpoint: Change from Week 24, D1 in serum phosphorus levels at Week 27, D1 – a superiority comparison between the PA21 MD group and the PA21 LD control group (fixed dose of 1.25 g/day) in the primary efficacy set (PES) of subjects on HD (D1 refers to the first dialysis session of the week).</p>

III. Site Selection/Rationale

We do not have any specific reasons for the selected sites.

Domestic Inspections:

Reasons for inspections (please check all that apply):

- Enrollment of large numbers of study subjects
- High treatment responders (specify):
- Significant primary efficacy results pertinent to decision-making
- There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, significant human subject protection violations or adverse event profiles.
- Other (specify):

International Inspections:

Reasons for inspections (please check all that apply):

- There are insufficient domestic data
- Only foreign data are submitted to support an application
- Domestic and foreign data show conflicting results pertinent to decision-making
- There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, or significant human subject protection violations.
- Other (specify) (Examples include: Enrollment of large numbers of study subjects and site specific protocol violations. This would be the first approval of this new drug and most of the limited experience with this drug has been at foreign sites, it would be desirable to include one foreign site in the DSI inspections to verify the quality of conduct of the study).

IV. Tables of Specific Data to be Verified (if applicable)

If you have specific data that needs to be verified, please provide a table for data verification, if applicable.

Should you require any additional information, please contact Anna Park, R.Ph.,RAC at 301-796-1129 or Shen Xiao, MD at 301-796-1312.

Concurrence: (as needed)

Shen Xiao, M.D. Cross-Discipline Team Leader & Medical Reviewer

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/s/

ANNA J PARK
03/20/2013

**REQUEST FOR OPDP (previously DDMAC) LABELING REVIEW
CONSULTATION**

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

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

TO: CDER-DDMAC-RPM	FROM: (Name/Title, Office/Division/Phone number of requestor) Anna Park/ODE1/DCRP/(301)796-1129
------------------------------	--

REQUEST DATE March 20, 2013	IND NO.	NDA/BLA NO. 205109	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW)
--------------------------------	---------	-----------------------	---

NAME OF DRUG PA21	PRIORITY CONSIDERATION Standard Review	CLASSIFICATION OF DRUG Phosphate binder	DESIRED COMPLETION DATE September 23, 2013
----------------------	---	--	---

NAME OF FIRM: Vifor Fresenius Medical Care Renal Pharma France Attention: Ms. Florence Dupre President of VMCRP France 12, Rue de la Chaussee d'Antin Paris, France, 75009 US Agent: Fresenius Medical Care North America Ruth Turner, Director of Regulatory Affairs – Pharma 920 Winter Street, Waltham, MA 02451	PDUFA Date: December 1, 2013
---	-------------------------------------

TYPE OF LABEL TO REVIEW

TYPE OF LABELING: (Check all that apply) <input checked="" type="checkbox"/> PACKAGE INSERT (PI) <input type="checkbox"/> PATIENT PACKAGE INSERT (PPI) <input checked="" type="checkbox"/> CARTON/CONTAINER LABELING <input type="checkbox"/> MEDICATION GUIDE <input type="checkbox"/> INSTRUCTIONS FOR USE(IFU)	TYPE OF APPLICATION/SUBMISSION <input checked="" type="checkbox"/> ORIGINAL NDA/BLA <input type="checkbox"/> IND <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> SAFETY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> PLR CONVERSION	REASON FOR LABELING CONSULT <input checked="" type="checkbox"/> INITIAL PROPOSED LABELING <input type="checkbox"/> LABELING REVISION
--	--	---

EDR link to submission: Please review the PI and carton/container labels for this NDA, PA21. This NDA was submitted on February 1, 2013 and the PDUFA goal date is December 1, 2013.
EDR link to submission: <\\cdsesub1\EVSPROD\NDA205109>

Please Note: There is no need to send labeling at this time. OPDP reviews substantially complete labeling, which has already been marked up by the CDER Review Team. After the disciplines have completed their sections of the labeling, a full review team labeling meeting can be held to go over all of the revisions. Within a week after this meeting, "substantially complete" labeling should be sent to OPDP. Once the substantially complete labeling is received, OPDP will complete its review within 14 calendar days.

COMMENTS/SPECIAL INSTRUCTIONS:
 Mid-Cycle Meeting: **July 2, 2013**
 Labeling Meetings: **July 9, 2013, August 12, 2013 and September 3, 2013**
 Wrap-Up Meeting: **September 30, 2013**

SIGNATURE OF REQUESTER
Anna Park

SIGNATURE OF RECEIVER	METHOD OF DELIVERY (Check one) <input type="checkbox"/> eMAIL <input checked="" type="checkbox"/> DARRTS
-----------------------	--

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ANNA J PARK
03/20/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): Mail: OSE		FROM: Anna Park/OND1/DCRP/(301)796-1129		
DATE March 13, 2013	IND NO.	NDA NO 205109	TYPE OF DOCUMENT Electronic	DATE OF DOCUMENT 2/1/13
NAME OF DRUG PA21	PRIORITY CONSIDERATION Routine	CLASSIFICATION OF DRUG Phosphate binder	DESIRED COMPLETION DATE September 23, 2013	
NAME OF FIRM: Vifor Fresenius Medical Care Renal Pharma France Attention: Ms. Florence Dupre, President of VFMCRP France 12, Rue de la Chaussee d'Antin Paris, France, 75009 US Agent: Fresenius Medical Care North America Ruth Turner, Director of Regulatory Affairs – Pharma 920 Winter Street, Waltham, MA 02451				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input checked="" type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: Please review the labels for this NDA. This NDA was submitted on February 1, 2013 and the PDUFA goal date is December 1, 2013. EDR link to submission: \\cdsesub1\EVSPROD\NDA205109				
SIGNATURE OF REQUESTER Anna Park		METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input checked="" type="checkbox"/> DARRTS		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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/s/

ANNA J PARK
03/14/2013

Park, Anna

From: Park, Anna
ent: Thursday, February 14, 2013 10:30 AM
to: 'Ruth.S.Turner@fmc-na.com'
Subject: NDA 205109

Dear Ruth,

I hope this email finds you well.

I've been going over your NDA application and could not locate the Debarment Certification. Do you know where it is located?

Thanks.
anna



NDA 205109

GENERAL ADVICE

Vifor Fresenius Medical Care Renal Pharma
Attention: Ms. Florence Dupre
President of VFMCRP France
12, Rue de la Chaussee d'Antin
Paris, France, 75009

Dear Ms. Dupre,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PA21 [REDACTED] ^{(b) (4)} Chewable Tablets, 500 mg.

We have reviewed your application and have concluded that PA21 [REDACTED] ^{(b) (4)} [REDACTED] is not a new molecular entity (NME) and will not be reviewed under the Program.

If you have any questions, please call Anna Park, Regulatory Project Manager, at (301) 796-1129.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: Fresenius Medical Care North America
Attention: Michael Bauer, Ph.D.
U.S. Agent for Vifor Fresenius Medical Care Renal Pharma
920 Winter Street
Waltham, MA 02451

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/s/

NORMAN L STOCKBRIDGE
02/13/2013



NDA 205109

NDA ACKNOWLEDGMENT

Vifor Fresenius Medical Care Renal Pharma France
Attention: Ms. Florence Dupre
President of VFMCRP France
12, Rue de la Chaussee d'Antin
Paris, France, 75009

Dear Ms. Dupre:

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

Name of Drug Product: PA21 [REDACTED] ^{(b) (4)} Chewable Tablets, 500 mg

Date of Application: January 31, 2013

Date of Receipt: February 1, 2013

Our Reference Number: NDA 205109

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 2, 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).

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

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

Food and Drug Administration
Center for Drug Evaluation and Research
Division of 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. Please note that secure email may not be used for formal regulatory submissions to applications.

If you have any questions, please contact:

Anna Park, R.Ph., RAC
Regulatory Health Project Manager
(301) 796-1129

Sincerely,

{See appended electronic signature page}

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

cc: Fresenius Medical Care North America
Attention: Michael Bauer, Ph.D.
U.S. Agent for Vifor Fresenius Medical Care Renal Pharma
920 Winter Street
Waltham, MA 02451

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/s/

EDWARD J FROMM
02/07/2013