

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-250

ADMINISTRATIVE DOCUMENTS

RECORD OF TELEPHONE CONVERSATION

<p>Reference is made to the deficiency letters dated October 25, 2000 and to the firm's fax dated November 2, 2000. The firm requested clarification on 3 deficiencies.</p>	<p>DATE: November 20, 2000</p>
<p>It was noted that the firm's amendment for ANDA 75-181 dated October 2, 2000 (received by document room October 23, 2000) will be reviewed in the next chemistry cycle.</p>	<p>ANDA NUMBER: 75-181 and 75-250</p>
<p>Deficiency 11: The proposed protocol is acceptable if the method has been validated. The firm was reminded of USP <661> procedures for PET.</p>	<p>PRODUCT NAME: Prednisolone Sodium Phosphate Syrup, 5 mg/5 mL and 15 mg/5 mL</p>
<p>Deficiency 10: Stability data and data from deficiency #11 will be considered when the Agency reviews the firm's amendment.</p>	<p>FIRM NAME: Kiel Laboratories, Inc. (for WE Pharmaceuticals)</p>
<p>Deficiency 5: The firm was asked to provide batch analyses from the supplier to support and justify their current drug substance specifications.</p>	<p>FIRM REPRESENTATIVE: Greg Thomas, VP of R&D; Tanyja Porcha Reg Affairs</p>
	<p>PHONE NUMBER: 770-534-0079</p>
	<p>FDA REPRESENTATIVES: Dave Gill Shing Hou Liu Ruby Yu</p>
	<p>SIGNATURES: Dave Gill <i>DS Gill</i> Shing Hou Liu <i>S.H. Liu 11/20/00</i> Ruby Yu <i>Ryu 11-20-00</i></p>

CC: ANDA 75-181 and 75-250
Telecon Binder

V:\FIRMSNZ\WE\TELCONS\75181.75250.tc.112000.doc

RECORD OF TELEPHONE CONVERSATION

<p>The firm was asked to amend their ANDAs as follows:</p> <p>Please establish a quantitative color test, such as APHA color test, and set a limit for your finished product release and stability program.</p>	<p style="text-align: center;">DATE: August 30, 2001</p>
	<p style="text-align: center;">ANDA NUMBER: 75-181 and 75-250</p>
	<p style="text-align: center;">PRODUCT NAME: Prednisolone Sodium Phosphate Syrup, 5 mg/5 mL and 15 mg/5 mL</p>
	<p style="text-align: center;">FIRM NAME: Kiel Laboratories, Inc. (for WE Pharmaceuticals)</p>
	<p style="text-align: center;">FIRM REPRESENTATIVE: Jeffrey S. Kiel</p>
	<p style="text-align: center;">PHONE NUMBER: 770-534-0079</p>
	<p style="text-align: center;">FDA REPRESENTATIVES: Steve Sherken, Acting TL Upinder Atwal, Chemist Ruby Yu, PM</p>
	<p style="text-align: center;">SIGNATURES:</p> <p>Steve Sherken <i>Steve Sherken</i> 8/30/01 Upinder Atwal <i>Upinder Atwal</i> 8/30/01 Ruby Yu <i>Ruby Yu</i> 8/30/01</p>

CC: ANDA 75-181 and 75-250
Telecon Binder

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-250

CORRESPONDENCE

OK to File
S. M. S. 11/10/97



Allergy/Asthma Products

November 10, 1997

Mr. Douglas Sporn
Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RECEIVED

NOV 14 1997

GENERIC DRUGS

RE: Original ANDA Submission for _____ (prednisolone sodium phosphate, USP) Syrup, 15mg/5mL

Dear Mr. Sporn:

WE Pharmaceuticals, Inc. (WE) submits today an original abbreviated new drug application (ANDA) seeking approval to market _____ (prednisolone sodium phosphate, USP) Syrup, 15mg/5mL that is bioequivalent to the listed drug, Pediapred® (prednisolone sodium phosphate, USP) Oral Solution, manufactured by Fisons pursuant to NDA# 19-157.

The facility for manufacturing of this dosage form is Kiel Laboratories, Inc., located at 2225 Centennial Drive in Gainesville, Georgia.

_____ (prednisolone sodium phosphate, USP) Syrup, 15mg/5mL is stable and a two year expiration dating is requested for all package sizes.

This ANDA is submitted in one (1) volume. WE is filing an archival copy (blue folders) of this application that contains all the information required in the ANDA and a technical review copy (red folders) containing all the information in the archival copy. Also, additional copies of the method validation reports are included in separate binders of this submission.

For more detailed information on the organization of this ANDA, please refer to the "Executive Summary - Organization of the ANDA" which follows this letter.

Page 2

To: Mr. Douglas L. Sporn

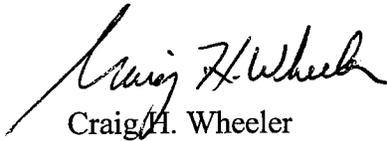
Subject: ANDA for _____ (prednisolone sodium phosphate, USP) Syrup,
15mg/5mL

We certify that a true copy of the technical section described in 21 CFR 314.50(d)(1), the chemistry, manufacturing, and controls section of this submission, has been provided to the San Diego District Office of the Food and Drug Administration.

Please direct any written communications regarding this ANDA to me at the below address. If you have any questions or require any additional information, please feel free to contact Jeffrey S. Kiel, President, Kiel Laboratories, Inc. at (770)534-0079.

Thank you for your prompt handling of this application.

Sincerely,



Craig H. Wheeler
President

ANDA 75-250

WE Pharmaceuticals, Inc.
Attention: Craig H. Wheeler
P.O. Box 1142
Ramona CA 92065



DEC 11 1997

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Prednisolone Sodium Phosphate Syrup,
15 mg/5 mL

DATE OF APPLICATION: November 10, 1997

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 14, 1997

We will correspond with you further after we have had the opportunity to review your application.

Please identify any communications concerning this application with the number shown above.

Should you have questions concerning this application contact:

Jim Wilson
Project Manager
(301) 827-5848

Sincerely yours,

A handwritten signature in dark ink, appearing to read "Jerry Phillips", written over the typed name.

Jerry Phillips
Director,
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-250
DUP/Jacket
Division File
HFD-82
Field Copy
HFD-330
HFD-600/Reading File
HFD-610/J.Phillips
HFD-615/MBennett

Endorsements:

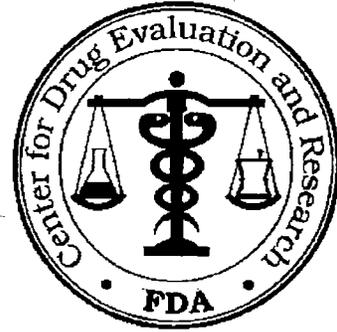
HFD-615/PRickman, Chief, ESB *W. Prickman*
HFD-615/SMiddleton, CSO *J. Middleton*
HFD-623/VSayed Sup. Chemistry
X:\NEW\FIRMSNZ\WE\LTRS&REV\75250.ACK
F/T by/njg/12/4/97
ANDA Acknowledgment Letter!

date/ *12/10/97*
date/ *12-4-97*
date/

MAJOR AMENDMENT

MAY 28 1998

ANDA 75-250



OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

TO: APPLICANT: WE Pharmaceuticals
ATTN: Craig H. Wheeler

PHONE: ~~619~~ 788-9155
FAX: ~~619~~ 788-9445

760

760

FROM: James Wilson

PROJECT MANAGER (301) 827-5848

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated November 10, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Prenisolone Sodium Phosphate, USP, Syrup, 15 mg/ 5 mL.

Reference is also made to your amendment(s) dated .

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (8 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance.

SPECIAL INSTRUCTIONS:

cme, Labeling and Bioequivalency comments are attached
ms 5/2/98

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address..

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of trade secret and/or

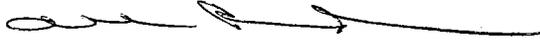
confidential commercial

information from

5/28/1998 FDA FAX

2. All DMFs referenced in this ANDA have to be found satisfactory at the time of approval of the ANDA. Some of the DMF holders may have to be inspected by our Division of Manufacturing and Product Quality. Any unsatisfactory review/evaluation will delay the approval of the ANDA.

Sincerely yours,



✓ Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

**REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 75-250

Date: November 10, 1997

Applicant's Name: WE Pharmaceuticals, Inc.

Established Name: _____ syrup {Prednisolone Sodium
Phosphate oral solution, 15 mg (base)/5 mL}

Labeling Deficiencies:

1. GENERAL COMMENTS

We acknowledge your proposal for a combined package insert for your two separate applications for different strengths. Please note that if these applications are not approved at the same time, further revisions may be necessary prior to approval.

2. CONTAINER - _____ 240 mL _____

- a. Revise the expression of the strength to read as follows:

15 mg/5 mL* [add "*"]

- b. We encourage you to differentiate your drug products of different strengths by using a boxing and/or contrasting colors, or some other means.
- c. *Each 5 mL (teaspoonful) ... [add "*" at the beginning]
- d. Revise to read "USUAL DOSAGE" rather than _____.
- e. Revise the storage requirement to read:

... to 25°C (39°F to 77°F). May be refrigerated. [rather than _____ and add "May be refrigerated."]
- f. We encourage the inclusion of the statement

"Keep tightly closed and out of the reach of children." as appears on the innovator's container labels and your package insert labeling.

g.



3. INSERT

a. GENERAL

The following comments are based on the most recently approved labeling of the reference listed drug, Pediapred® (Fisons; approved November 22, 1993, revised July, 1993). In addition, other changes are indicated.

b. DESCRIPTION

i. Second paragraph:

- A) Please alphabetize the listing of inactive ingredients.
- B) Revise to express the alcohol content of your product in terms of percent volume (v/v) of absolute alcohol as found on your container labels. You are referred to 21 CFR 201.10(d)(2) for guidance.

C)



- D) You may delete "purified water".

ii. Third paragraph:

- A) We encourage you to revise the chemical name to be same as the second name

appearing in the official monograph for prednisolone sodium phosphate in USP 23.

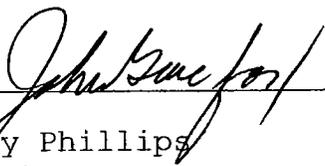
- B) The molecular formula ... [rather than "empirical"]
 - C) Revise the molecular weight to read "484.40" to be in accordance with USP 23.
- c. CLINICAL PHARMACOLOGY - First paragraph, last sentence:
- ... anti-insulin activity; increase catabolism of protein; increased lipolysis; stimulation of fat synthesis and storage; increased glomerular ...
- d. INDICATIONS AND USAGE - 3. Collagen Diseases:
- ... systemic dermatomyositis (polymyositis); acute rheumatic carditis.
- e. WARNINGS
- Delete the last paragraph.
- f. HOW SUPPLIED
- i. First sentence - Revise to read as follows:
... pink to purple colored, grape flavored oral solution.
 - ii. We encourage the inclusion of the "Dispense in" statement as appears on the container labels.

Please revise your labels and labeling, as instructed above, and submit in final print, or in draft if you prefer.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with the last submitted labeling with all differences annotated and

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with the last submitted labeling with all differences annotated and explained.



Jerry Phillips
Director

Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-250

APPLICANT:WE Pharmaceuticals, Inc.

DRUG PRODUCT: ~~_____~~ 15 mg/5 ml syrup

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,



Dale P. Conner, Pharm.D.
Director Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-250

CERTIFIED MAIL-RETURN RECEIPT REQUESTED

WE Pharmaceuticals, Inc.
Attention: Craig H. Wheeler
P.O. Box 1142
Ramona, CA 92065

MAY 9 2000

Dear Sir:

This letter is in reference to your Abbreviated New Drug Application (ANDA) dated November 10, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Prednisolone Sodium Phosphate Syrup, 15 mg(base)/5 mL.

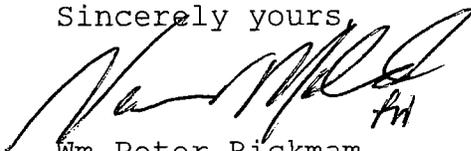
We refer you to our "Not Approvable" letter dated May 28, 1998, which detailed the deficiencies identified during our review of your ANDA. The Agency may consider an ANDA applicant's failure to respond to a "Not Approvable" letter within 180 days to be a request by the applicant to withdraw the ANDA under 314.120(b). Your amendment to the application is overdue. You must amend your application within 10 days of receipt of this letter. Otherwise, an action to withdraw the application will be initiated per 21 CFR 314.99.

If you do not wish to pursue approval of this application at this time, you should request withdrawal in accord with 21 CFR 314.65. A decision to withdraw the application would be without prejudice to refiling.

Please send all correspondence to the following address:

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Sincerely yours,



Wm Peter Rickmam
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA # 75-250
DUP/Division File
HFD-610/PRickman

Endorsement:

HFD-617/NMahmud, Chief, RSB, 

date 5/9/00

HFD-617/SMiddleton, CSO, S. Middleton

date 5/9/00

Word File

V:\FIRMSNZ\WE\LTRS&REV\75250.OTH

F/T by mjl\5\4\00

10 DAY LETTER!



PHARMACEUTICALS, INC.

Allergy/Asthma Products

P.O. Box 1142, Ramona, California 92065 • (760) 788-9155 • (800) 262-9555 • FAX (760) 788-9445 • <http://www.weez.com>

May 26, 2000

Mr. Douglas Sporn
Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT

NP AC

RE: ANDA 75-250 Major Amendment Response Prednisolone Sodium Phosphate, Syrup, 15mg/5mL

Dear Mr. Sporn:

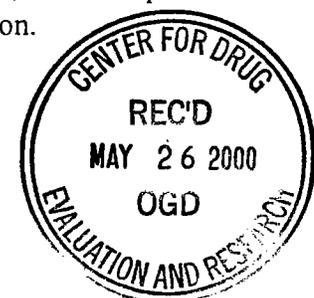
Reference is made to your "Not Approvable" facsimile received on May 28, 1998, Prednisolone Sodium Phosphate, Syrup, 15mg/5mL. A copy of the facsimile is included in this application.

WE Pharmaceuticals, Inc. (WE) submits today a major amendment response to the abbreviated new drug application (ANDA) number 75-250 seeking approval to market Prednisolone Sodium Phosphate, Syrup, 15mg/5mL.

The facility for manufacturing of this dosage form is Kiel Laboratories, Inc., located at 2225 Centennial Drive in Gainesville, Georgia.

This ANDA major amendment response is submitted in one (1) volume. WE is filing an archival copy (blue folders) of this application that contains all the information required in the ANDA and a technical review copy (red folders) containing all the information in the archival copy.

We certify that a true copy of the technical section described in 21 CFR 314.50(d)(1), the chemistry, manufacturing, and controls section of this submission, has been provided to the San Diego District Office of the Food and Drug Administration.



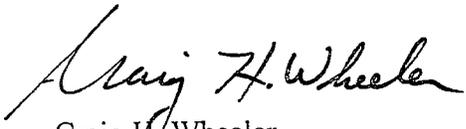
Page 2

To: Mr. Douglas L. Sporn
Subject: ANDA 75-250 Major Amendment Response for Prednisolone Sodium
Phosphate, Syrup, 15mg/5mL

Please direct any written communications regarding this ANDA to me at the below
address. If you have any questions or require any additional information, please feel free
to contact Jeffrey S. Kiel, President, Kiel Laboratories, Inc. at (770)534-0079.

Thank you for your prompt handling of this application.

Sincerely,

A handwritten signature in cursive script that reads "Craig H. Wheeler". The signature is written in black ink and is positioned above the printed name and title.

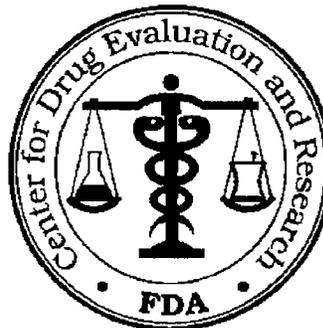
Craig H. Wheeler
President

MAJOR AMENDMENT

25

ANDA 75-250

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)



TO: APPLICANT: WE Pharmaceuticals, Inc.
ATTN: Craig Wheeler

PHONE: ⁷⁶⁰619-788-9155
FAX: 760-788-4517

FROM: Ruby Yu

PROJECT MANAGER (301) 827-5848

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated November 10, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Prednisolone Sodium Phosphate Oral Solution, 15 mg/5 mL.

Reference is also made to your amendment(s) dated May 26, 2000.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (3 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. **If this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance.**

SPECIAL INSTRUCTIONS:

Chemistry comments provided. Bioequivalency and Labeling comments will be provided when the reviews are completed.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

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Ryu 10-25-00

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of trade secret and/or

confidential commercial

information from

10/25/2000 FDA FAX



P.O. Box 1142, Ramona, California 92065 • (760) 788-9155 • (800) 262-9555 • FAX (760) 788-9445 • <http://www.weez.com>

December 20, 2000

ORIG AMENDMENT

N/A/C

Mr. Gary Buehler
Acting Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: ANDA 75-250 – Prednisolone Sodium Phosphate Syrup, 15 mg/5 mL

Subj.: Major Amendment Response

Dear Mr. Buehler:

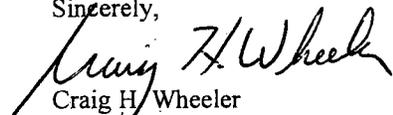
Reference is made to a “Not Approvable” facsimile dated October 25, 2000 concerning major deficiencies in our Abbreviated New Drug Application 75-250 for Prednisolone Sodium Phosphate Syrup, 15 mg/5 mL.

In this **Major Amendment** we now respond to all the deficiencies listed in the referenced letter. This **Major Amendment** is submitted in one (1) volume, an archival copy (blue) and a technical review copy (red).

The manufacturing facility for the finished product is Kiel Laboratories, Inc., located at 2225 Centennial Drive, Gainesville, GA. We certify that a true copy of this amendment has been provided to the Food and Drug Administration, Atlanta District Office, Atlanta, GA.

Please direct any written communications regarding this ANDA to me at the below address. If you have any technical questions or require any additional information, please feel free to contact Jeffrey S. Kiel, President, Kiel Laboratories, Inc. at (770) 534-0079.

Sincerely,


Craig H. Wheeler
President





Allergy/Asthma Products

P.O. Box 1142, Ramona, California 92065 • (760) 788-9155 • (800) 262-9555 • FAX (760) 788-9445 • http://www.weez.com

March 16, 2001

Mr. Gary Buehler
Acting Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N/A/C

RE: Amendment to ANDA 75-250, Prednisolone Sodium Phosphate Syrup, 15 mg/5 mL

Dear Mr. Buehler:

WE Pharmaceuticals, Inc. (WE) is submitting an Amendment to Abbreviated New Drug Application 75-250, Prednisolone Sodium Phosphate Syrup, 15 mg/5 mL. This Amendment is submitted in one (1) volume, with copies in an archival (blue) folder and a technical review (red) folder.

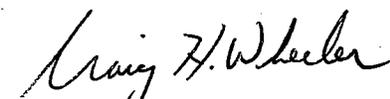
In this Amendment, WE provides additional information in support of a Major Amendment Response submitted January 2, 2001, as response to a "Not Approvable" facsimile dated October 25, 2000. Also in this Amendment, WE withdraws _____

_____ A copy of the specification was provided in Major Amendment Response dated May 26, 2000. This Amendment also includes additional information regarding contract laboratories responsibilities. And this Amendment also includes a correction to Raw Material Specification _____

The manufacturing facility for the finished dosage form is Kiel Laboratories™, located at 2225 Centennial Drive, Gainesville, GA. WE Pharmaceuticals is forwarding a true copy of this Amendment to the Atlanta District Office, Food and Drug Administration, and certifies that the information contained in this true copy is the same as that submitted to FDA Headquarters.

Please direct any written communications regarding this Amendment to me at the address below. If you have any technical questions, or require any additional information, please contact Jeffrey S. Kiel, President, Kiel Laboratories™ at 2225 Centennial Dr., Gainesville, GA 30504 or at (770) 534-0079.

Sincerely,


Craig H. Wheeler
President

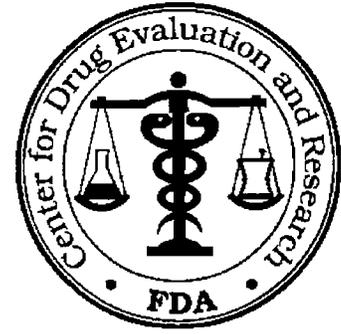


FAX AMENDMENT

ANDA 75-250

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

JUL - 3 2001



TO: APPLICANT: WE Pharmaceuticals, Inc.

TEL: 760-788-9155

ATTN: Craig H. Wheeler

FAX: 760-788-4517

FROM: Ruby Yu

PROJECT MANAGER: 301-827-5848

Dear ^{Sir}~~Madam~~:

This facsimile is in reference to your abbreviated new drug application dated November 10, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Prednisolone Sodium Phosphate Oral Solution 15 mg/5 mL.

Reference is also made to your amendment(s) dated: December 20, 2000; and March 16, 2001.

Attached are 1 pages of minor deficiencies and/or comments that should be responded to within 30 calendar days from the date of this document. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed. Your complete response should be (1) faxed directly to our document control room at 301-827-4337, (2) mailed directly to the above address, and (3) the cover sheet should be clearly marked a FAX AMENDMENT.

Please note that if you are unable to provide a complete response within 30 calendar days, the file on this application will be closed as a MINOR AMENDMENT and you will be required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Accordingly, a response of greater than 30 days should be clearly marked MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. Facsimiles or incomplete responses received after 30 calendar days will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. Further if a major deficiency is cited in the bioequivalence review, the subsequent Not Approvable letter will request that the reply be declared a MAJOR AMENDMENT.

SPECIAL INSTRUCTIONS:

Chemistry comments provided. Labeling comments will follow when the review is completed.

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

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Ry
7/3/01

JUL -3 2001

38. Chemistry Comments to be Provided to the Applicant

ANDA: 75-250 APPLICANT: WE Pharmaceuticals Inc.

DRUG PRODUCT: Prednisolone Sodium Phosphate Oral Solution, 15 mg(base)/5 mL

The deficiencies presented below represent FAX deficiencies.

A. Deficiencies:

1.

2.

3.

B. In addition to responding to the deficiencies presented above, Please note and acknowledge the following comments in your response:

1. Labeling portion of your application is under review. Deficiencies, if any, will be conveyed to you under separate cover.

Sincerely yours,



Rashmikant M. Patel, Ph.D.

Director

Division of Chemistry I

Office of Generic Drugs

Center for Drug Evaluation and Research

Kiel Laboratories™
2225 Centennial Drive
Gainesville, GA 30504
Ph: 770-534-0079
FAX: 770-534-0229



FAX

ORIG AMENDMENT
N/FA

To: Mr. Gary Buehler From: Swarna Mukund
 Company: Document control for FDA E.mail: swarnamukund@hotmail.com
 FAX: 301-827-4337 Pages 60 (including cover)
 Phone: 301-827-5848 Date: 07/31/01
 Re: FAX AMENDMENT cc: _____

Urgent For Review Please Comment Please Reply

Message:

Please find enclosed responses to the facsimile deficiencies dated July 3, 2001 for ANDA 75-250 for Prednisolone Sodium Phosphate Syrup 15 mg/ mL.

Sincerely,

Swarna Mukund
Swarna Mukund

• **Comments:** The information contained in this document is confidential and may not be used except for the intended purpose. If the reader of this message is not the intended recipient or a duly authorized agent responsible for delivering it to the intended recipient, you are hereby notified that this document has been received in error. Furthermore, any review, dissemination, distribution or copying of this message is strictly prohibited. If you have received this communication in error, please notify us immediately by telephone.



Allergy/Asthma Products

P.O. Box 1142, Ramona, California 92065 • (760) 788-9155 • (800) 262-9555 • FAX (760) 788-9445 • <http://www.weez.com>

July 31, 2001

Mr. Gary Buehler
Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 0855-2773

NC

SUBJECT: FACSIMILE AMENDMENT TO ANDA 75-250
RE: Prednisolone Sodium Phosphate, Syrup, 15 mg/ 5 mL

Dear Mr. Buehler:

Reference is made to your facsimile dated July 3, 2001 regarding minor deficiencies for Prednisolone Sodium Phosphate, Syrup, 15 mg/ 5 mL, ANDA 75-250. In this amendment, we are responding to the chemistry deficiencies communicated in the facsimile amendment notification.

As required by 21 CFR 314.94(D)(5), WE Pharmaceuticals, Inc., (WE) is forwarding a true copy of the amendment, including a completed copy of FDA form 356h. This facsimile amendment is submitted in one (1) volume. WE is filing an archival copy (blue folder) and a technical review copy (red) of this submission.

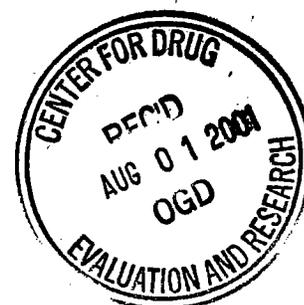
The manufacturing facility for the finished product is Kiel Laboratories, Inc., located at 2225 Centennial Drive, Gainesville, GA. We certify that a true copy of this amendment has been provided to the Food and Drug Administration, Atlanta District office, Atlanta, GA.

Please direct any written communication regarding this ANDA to me at the above address. If you have any technical questions or require additional information, please feel free to contact Jeffrey S. Kiel, President, Kiel Laboratories, Inc., at 770-534-0079.

Sincerely,

A handwritten signature in black ink that reads 'Craig H. Wheeler'.

Craig H. Wheeler
President





Allergy/Asthma Products

P.O. Box 1142, Ramona, California 92065 • (760) 788-9155 • (800) 262-9555 • FAX (760) 788-9445 • <http://www.weez.com>

NC
NEW CORRESP

Aug 9, 2001

Mr. Gary Buehler
Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 0855-2773

SUBJECT: ANDA METHOD VALIDATION LETTER

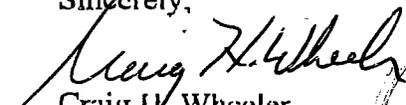
RE: Prednisolone Sodium Phosphate, Syrup, 15 mg/ 5 ml., ANDA 75-250

Dear Mr. Buchler,

We have sent the method validation package and the samples regarding Prednisolone Sodium Phosphate, Syrup, 15 mg/ 5 ml., ANDA 75-250 to Ms. Emma S. Aranda, supervisory chemist/Drug chemistry, Food and Drug Administration, Pacific Regional Laboratory - SouthWest 1521 W. Plco Blvd, Los Angeles, CA 90015 as per the 'ANDA Method Validation Letter' dated July 31, 2001. In this package we are sending true copies of the same documents for your records. We have also sent copies of the same documents to the Food and Drug Administration, Atlanta district office, Atlanta, GA.

Please direct any written communication regarding this ANDA to me at the above address. If you have any technical questions or require additional information, please feel free to contact Jeffrey S. Kiel, President, Kiel Laboratories, Inc., at 770-534-0079.

Sincerely,


Craig I. Wheeler
President



Fax Cover Sheet



**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Rockville, Maryland**

This document is intended only for the use of the party to whom it is addressed and may contain information that is privileged, confidential, and protected from disclosure under applicable law. If you are not the addressee, or a person authorized to deliver the document to the addressee, this communication is not authorized. If you have received this document in error, immediately notify us by telephone and return it to us at the above address by mail. Thank you.

To: Craig H. Wheeler
WE Pharmaceuticals, Inc.

Fax: 760-788-4517 **Phone:** 760-788-9155

From: Debra M. Catterson
Labeling Reviewer

Fax: 301-443-3847 **Phone:** 301-827-5846

Number of Pages (including cover sheet): 8 **Date:** August 10, 2001

Comments:

Dear Mr. Wheeler,

Attached is the labeling review of your May 26, 2000 submission for ANDA 75-250 for Prednisolone Sodium Phosphate Oral Solution, 15 mg (base)/5 mL.

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

Sincerely,

Debra M. Catterson

**REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 75-250 Date of Submission: May 26, 2000 (**Major Amendment**)
Applicant's Name: WE Pharmaceuticals, Inc.
Established Name: Prednisolone Sodium Phosphate Oral Solution, 15 mg (base)/5 mL

Labeling Deficiencies:

1. **NOTE:** We note in your May 26, 2000 submission that you proposed to _____

2. **CONTAINER – bottles containing _____ 240 mL _____**
 - a. The established name for this drug product is "**Prednisolone Sodium Phosphate Oral Solution**". Please refer to the reference listed drug "Orapred" for guidance.

 - b. Side panel; Revise to read – [replace " _____ mg" with "20.2 mg"]

DESCRIPTION: *Each 5 mL (teaspoonful) contains prednisolone sodium phosphate 20.2 mg (15 mg prednisolone base) in a palatable solution.

3. **PACKAGE INSERT**

a. **GENERAL COMMENTS**

- i. Please revise your labeling to be in accordance with the most recently approved labeling for the new reference list Orapred® Oral Solution, 15 mg/5 mL (NDA 75-117; approved December 14, 2000), listed in the 2001 Orange Book, 21st edition (**See attached copy of this most recently approved labeling for Orapred® Oral Solution**)

In addition to the attached copy of the most recently approved labeling for the reference listed drug, Orapred®, please make the following revisions listed below.

- ii. The established name for this drug product is "prednisolone sodium phosphate oral solution". Therefore, replace "prednisolone sodium phosphate syrup" with "prednisolone sodium phosphate oral solution" throughout the text.

b. **DESCRIPTION**

- i. Revise the molecular weight to read "484.39" as it is listed in the reference listed drugs package insert and the USP.

- ii. We note that _____ is still listed in your DESCRIPTION section. However, it states in your Components and Compositions Statement that _____ has been replaced. Please revise and/or comment.

Please revise your labels and labeling, as instructed above, and submit in final print.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes-

http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

A handwritten signature in black ink, appearing to read "Wm. Peter Rickman", written over a horizontal line.

Wm. Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Attached: A copy of the most recently approved labels and labeling for, Orapred® Oral Solution, 15 mg/5 mL (NDA 75-177; approved December 14, 2000).

APPROVED

DEC 74 2000

Pharmacists: Dispense in tight, light-resistant glass or PET plastic containers as defined in USP.

Keep tightly closed and out of the reach of children.



NDC 59439-455-02

Equivalent to prednisolone
15 mg/5mL

Orapred[®]

(prednisolone sodium phosphate
oral solution)

Rx only

8 fl oz (237 mL)

Store refrigerated, 2-8°C (36-46°F)



For usual dosage and important prescribing information see accompanying package insert.

Description: Each 5 mL (teaspoonful) contains 20.2 mg prednisolone sodium phosphate (15 mg prednisolone base) in a palatable solution. Contains alcohol 2%.

Manufactured for
Ascent Pediatrics, Inc.
Wilmington, MA 01887
by
Lyne Laboratories, Inc.
Brockton, MA 02301

L2A0300

ment; acute or chronic solid organ rejection (with or without other agents).

CONTRAINDICATIONS

Systemic fungal infections.

Hypersensitivity to the drug or any of its components.

WARNINGS

General:

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated.

Endocrine:

Corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment.

Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in dosage.

Infections (general):

Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. There may be decreased resistance and inability to localize infection when corticosteroids are used. Infection with any pathogen including viral, bacterial, fungal, protozoan or helminthic infection, in any location of the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect humoral or cellular immunity, or neutrophil function. These infections may be mild to severe, and, with increasing doses of corticosteroids, the rate of occurrence of infectious complications increases. Corticosteroids may also mask some signs of infection after it has already started.

Viral Infections:

Chicken pox and measles for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In such children or adults who have not had the diseases, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chicken pox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information). If chicken pox develops, treatment with antiviral agents should be considered.

Special pathogens:

Latent disease may be activated or there may be an exacerbation of intercurrent infections due to pathogens, including those caused by *Candida*, *Mycobacterium*, *Amoeba*, *Toxoplasma*, *Pneumocystis*, *Cryptococcus*, *Nocardia*, etc.

Corticosteroids may activate latent amebiasis. Therefore, it is recommended that latent or active amebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or in any patient with unexplained diarrhea.

Similarly, corticosteroids should be used with great care in patients with known or suspected *Strongyloides* (threadworm) infestation. In such patients, corticosteroid-induced immunosuppression may lead to *Strongyloides* hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia.

Corticosteroids should not be used in cerebral malaria.

Tuberculosis:

The use of prednisolone in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy these patients should receive chemoprophylaxis.

Vaccination:

Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered, however, the response to such vaccines can not be predicted. Immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease.

Ophthalmic:

Use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to bacteria, fungi or viruses. The use of oral corticosteroids is not recommended in the treatment of optic neuritis and may lead to an increase in the risk of new episodes.

Corticosteroids should not be used in active ocular herpes simplex.

Cardio-renal:

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

PRECAUTIONS

General:

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.

Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy, most often for chronic conditions. Discontinuation of corticosteroids may result in clinical improvement.

Endocrine:

Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstated. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

Ophthalmic:

Intraocular pressure may become elevated in some individuals. If steroid therapy is continued for more than 6 weeks, intraocular pressure should be monitored.

Neuro-psychiatric:

Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis, they do not show that they affect the ultimate outcome or natural history of the disease. The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect. (See DOSAGE AND ADMINISTRATION.)

An acute myopathy has been observed with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g., myasthenia gravis), or in patients receiving concomitant therapy with neuromuscular blocking drugs (e.g., pancuronium). This acute

myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriplegia. Elevation of creatinine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Gastrointestinal:

Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer.

Signs of peritoneal irritation following gastrointestinal perforation in patients receiving corticosteroids may be minimal or absent.

Cardio-renal:

As sodium retention with resultant edema and potassium loss may occur in patients receiving corticosteroids, these agents should be used with caution in patients with hypertension, congestive heart failure, or renal insufficiency.

Musculoskeletal:

Corticosteroids decrease bone formation and increase bone resorption both through their effect on calcium regulation (i.e., decreasing absorption and increasing excretion) and inhibition of osteoblast function. This, together with a decrease in the protein matrix of the bone secondary to an increase in protein catabolism, and reduced sex hormone production, may lead to inhibition of bone growth in children and adolescents and the development of osteoporosis at any age. Special consideration should be given to patients at increased risk of osteoporosis (i.e., postmenopausal women) before initiating corticosteroid therapy.

Information for Patients:

Patients should be warned not to discontinue the use of Orapred abruptly or without medical supervision, to advise any medical attendants that they are taking Orapred and to seek medical advice at once should they develop fever or other signs of infection.

Persons who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles. Patients should also be advised that if they are exposed, medical advice should be sought without delay.

Drug Interactions:

Drugs such as barbiturates, phenytoin, ephedrine, and rifampin, which induce hepatic microsomal drug metabolizing enzyme activity may enhance metabolism of prednisolone and require that the dosage of Orapred be increased.

Increased activity of both cyclosporin and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use.

Estrogens may decrease the hepatic metabolism of certain corticosteroids thereby increasing their effect.

Ketoconazole has been reported to decrease the metabolism of certain corticosteroids by up to 60% leading to an increased risk of corticosteroid side effects.

Coadministration of corticosteroids and warfarin usually results in inhibition of response to warfarin, although there have been some conflicting reports. Therefore, coagulation indices should be monitored frequently to maintain the desired anticoagulant effect.

Concomitant use of aspirin (or other non-steroidal anti-inflammatory agents) and corticosteroids increases the risk of gastrointestinal side effects. Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. The clearance of salicylates may be increased with concurrent use of corticosteroids.

When corticosteroids are administered concomitantly with

potassium-depleting agents (i.e., diuretics, amphotericin-B), patients should be observed closely for development of hypokalemia. Patients on digitalis glycosides may be at increased risk of arrhythmias due to hypokalemia.

Concomitant use of anticholinesterase agents and corticosteroids may produce severe weakness in patients with myasthenia gravis. If possible, anticholinesterase agents should be withdrawn at least 24 hours before initiating corticosteroid therapy.

Due to inhibition of antibody response, patients on prolonged corticosteroid therapy may exhibit a diminished response to live or inactivated vaccines. Corticosteroids may also potentiate the replication of some organisms contained in live attenuated vaccines. If possible, routine administration of vaccines or toxoids should be deferred until corticosteroid therapy is discontinued.

Because corticosteroids may increase blood glucose concentrations, dosage adjustment of antidiabetic agents may be required. Corticosteroids may suppress reactions to skin tests.

Pregnancy: Teratogenic effects: Pregnancy Category C.

Prednisolone has been shown to be teratogenic in many species when given in doses equivalent to the human dose. Animal studies in which prednisolone has been given to pregnant mice, rats, and rabbits have yielded an increased incidence of cleft palate in the offspring. There are no adequate and well-controlled studies in pregnant women. Orapred should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Infants born to mothers who have received corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Nursing Mothers:

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when Orapred is administered to a nursing woman.

Pediatric Use:

The efficacy and safety of prednisolone in the pediatric population are based on the well-established course of effect of corticosteroids which is similar in pediatric and adult populations. Published studies provide evidence of efficacy and safety in pediatric patients for the treatment of nephrotic syndrome (>2 years of age), and aggressive lymphomas and leukemias (>1 month of age). However, some of these conclusions and other indications for pediatric use of corticosteroid, e.g., severe asthma and wheezing, are based on adequate and well-controlled trials conducted in adults, on the premises that the course of the diseases and their pathophysiology are considered to be substantially similar in both populations.

The adverse effects of prednisolone in pediatric patients are similar to those in adults (see ADVERSE REACTIONS). Like adults, pediatric patients should be carefully observed with frequent measurements of blood pressure, weight, height, intraocular pressure, and clinical evaluation for the presence of infection, psychosocial disturbances, thromboembolism, peptic ulcers, cataracts, and osteoporosis. Children who are treated with corticosteroids by any route, including systemically administered corticosteroids, may experience a decrease in their growth velocity. This negative impact of corticosteroids on growth has been observed at low systemic doses and in the absence of laboratory evidence of HPA axis suppression (i.e., cosyntropin stimulation and basal cortisol plasma levels). Growth velocity may therefore be a more sensitive indicator of systemic corticosteroid exposure in children than some commonly used tests of HPA axis function. The linear growth of children treated with corticosteroids by any route should be monitored, and the potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the availability of other treatment alternatives. In order to minimize the potential growth effects of corticosteroids, children should be *titrated* to the lowest effective dose.

ADVERSE REACTIONS

(Listed alphabetically under each subsection)

Fluid and Electrolyte Disturbances: Congestive heart failure in susceptible patients; fluid retention; hypertension; hypokalemic alkalosis; potassium loss; sodium retention.

Cardiovascular: Hypertrophic cardiomyopathy in premature infants.

Musculoskeletal: Aseptic necrosis of femoral and humeral heads; loss of muscle mass; muscle weakness; osteoporosis; pathologic fracture of long bones; steroid myopathy; tendon rupture; vertebral compression fractures.

Gastrointestinal: Abdominal distention; elevation in serum liver enzyme levels (usually reversible upon discontinuation); pancreatitis; peptic ulcer with possible perforation and hemorrhage; ulcerative esophagitis.

Dermatologic: Facial erythema; increased sweating; impaired wound healing; may suppress reactions to skin tests; petechiae and ecchymoses; thin fragile skin; urticaria; edema.

Metabolic: Negative nitrogen balance due to protein catabolism.

Neurological: Convulsions; headache; increased intracranial pressure with papilledema (pseudotumor cerebri), usually following discontinuation of treatment; psychic disorders; vertigo.

Endocrine: Decreased carbohydrate tolerance; development of cushingoid state; hirsutism; increased requirements for insulin or oral hypoglycemic agents in diabetes; manifestations of latent diabetes mellitus; menstrual irregularities; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness; suppression of growth in children.

Ophthalmic: Exophthalmos; glaucoma; increased intraocular pressure; posterior subcapsular cataracts.

Other: Increased appetite; malaise; nausea; weight gain.

OVERDOSAGE

The effects of accidental ingestion of large quantities of prednisolone over a very short period of time have not been reported, but prolonged use of the drug can produce mental symptoms, moon face, abnormal fat deposits, fluid retention, excessive appetite, weight gain, hypertrichosis, acne, striae, ecchymosis, increased sweating, pigmentation, dry scaly skin, thinning scalp hair, increased blood pressure, tachycardia, thrombophlebitis, decreased resistance to infection, negative nitrogen balance with delayed bone and wound healing, headache, weakness, menstrual disorders, accentuated menopausal symptoms, neuropathy, fractures, osteoporosis, peptic ulcer, decreased glucose tolerance, hypokalemia, and adrenal insufficiency.

Hepatomegaly and abdominal distention have been observed in children.

Treatment of acute overdosage is by immediate gastric lavage or emesis followed by supportive and symptomatic therapy. For chronic overdosage in the face of severe disease requiring continuous steroid therapy the dosage of prednisolone may be reduced only temporarily, or alternate day treatment may be introduced.

DOSAGE AND ADMINISTRATION

The initial dose of Orapred may vary from 1.67 mL to 20 mL (5 to 60 mg prednisolone base) per day depending on the specific disease entity being treated. In situations of less severity, lower doses will generally suffice while in selected patients higher initial doses may be required. The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time, there is a lack of satisfactory clinical response, Orapred should be discontinued and the patient placed on other appropriate therapy. **IT SHOULD BE EMPHASIZED THAT DOSAGE REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE UNDER TREATMENT AND THE RESPONSE OF THE PATIENT.** After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. It should be kept in mind that constant monitoring is needed in regard to drug dosage. Included in the

situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment; in this latter situation it may be necessary to increase the dosage of Orapred for a period of time consistent with the patient's condition. If after long term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

In the treatment of acute exacerbations of multiple sclerosis daily doses of 200 mg of prednisolone for a week followed by 80 mg every other day or 4 to 8 mg dexamethasone every other day for one month have been shown to be effective.

In pediatric patients, the initial dose of Orapred may vary depending on the specific disease entity being treated. The range of initial doses is 0.14 to 2 mg/kg/day in three or four divided doses (4 to 60 mg/m²/day).

The standard regimen used to treat nephrotic syndrome in pediatric patients is 60 mg/m²/day given in three divided doses for 4 weeks, followed by 4 weeks of single dose alternate-day therapy at 40 mg/m²/day.

The National Heart, Lung, and Blood Institute (NHLBI) recommended dosing for systemic prednisone, prednisolone or methylprednisolone in children whose asthma is uncontrolled by inhaled corticosteroids and long-acting bronchodilators is 1-2 mg/kg/day in single or divided doses. It is further recommended that short course, or "burst" therapy, be continued until a child achieves a peak expiratory flow rate of 80% of his or her personal best or symptoms resolve. This usually requires 3 to 10 days of treatment, although it can take longer. There is no evidence that tapering the dose after improvement will prevent a relapse.

For the purpose of comparison, 5 mL of Orapred (20.2 mg prednisolone sodium phosphate) is equivalent to the following milligram dosage of the various glucocorticoids:

Cortisone, 75	Triamcinolone, 12
Hydrocortisone, 60	Paramethasone, 6
Prednisolone, 15	Betamethasone, 2.25
Prednisone, 15	Dexamethasone, 2.25
Methylprednisolone, 12	

These dose relationships apply only to oral or intravenous administration of these compounds. When these substances or their derivatives are injected intramuscularly or into joint spaces, their relative properties may be greatly altered.

HOW SUPPLIED

Each 5 mL (teaspoonful) of grape flavored solution contains 20.2 mg prednisolone sodium phosphate (15 mg prednisolone base).

Available as:

8 fl oz (237 mL) NDC 59439-455-02

16 fl oz (473 mL) NDC 59439-455-03

Dispense in tight, light-resistant glass or PET plastic containers as defined in USP.

Store refrigerated, 2-8°C (36-46°F)

Keep tightly closed and out of the reach of children.

Rx only

Revised March 8, 2000.

Manufactured for Ascent Pediatrics, Inc.,
Wilmington, MA 01887
by Lyne Laboratories, Inc., Brockton, MA 02301



KIEL LABORATORIES, INC.

September 10, 2001

Mr. Gary Buehler
Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

FA
ORIG AMENDMENT

TELEPHONE AMENDMENT

RE: ANDA 75-250, PREDNISOLONE SODIUM PHOSPHATE, USP, ORAL SOLUTION, 15mg/5 mL

WE Pharmaceuticals, Inc. (WE) is submitting a TELEPHONE AMENDMENT to Abbreviated New Drug Application 75-250, Prednisolone Sodium Phosphate, USP, Oral Solution, 15mg/5 mL. This amendment is submitted in one (1) volume, with copies in an archival (blue) folder and a technical review (red) folder.

In this Telephone Amendment, WE provides information in support of a request for additional specifications for the Prednisolone Sodium Phosphate, USP, Oral Solution, 15 mg/5mL. The request involved adding a specification for product color to the finished product specification, the stability protocol and a method to quantitatively measure and monitor the color.

This amendment contains a copy of the finished product specification including the requirement for color, a stability protocol including a color specification and a standard operating procedure for the test method to quantitatively measure color.

The manufacturing and packaging facility for the finished dosage form is Kiel Laboratories™ located at 2225 Centennial Drive, Gainesville, GA. WE Pharmaceuticals is forwarding a true copy of this Telephone Amendment to the Atlanta District Office, Food and Drug Administration, and certifies that the information contained in this true copy is the same as that submitted to FDA headquarters.

Please direct any written communications regarding this Amendment to me at the address below. If you have any technical questions, or require additional information, please contact me at Kiel Laboratories™ at (770) 534-0079.

Sincerely,



Thomas A. Dunkle
Regulatory Associate





Allergy/Asthma Products

P.O. Box 1142, Ramona, California 92065 • (760) 788-9155 • (800) 262-9555 • FAX (760) 788-9445 • <http://www.weez.com>
October 19, 2001

Mr. Gary Buehler
Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT

N/FA



2.
dc

SUBJECT: Labeling Deficiency Response, Patent Certification Statement, and
Additional Amendment TO ANDA 75-250
RE: Prednisolone Sodium Phosphate Oral Solution, 15mg/5mL

wrong submission -
this ANDA is
75-181

Dear Mr. Buehler,

Reference is made to your facsimile dated August 10, 2001 regarding deficiencies for Prednisolone Sodium Phosphate Oral Solution, 15mg(base)/5mL, ANDA 75-250 and telephone conversation requests of October 15, 2001. This ANDA is based on the reference listed drug, ORAPRED® (prednisolone sodium phosphate) Oral Solution, 15mg(base)/5mL by Ascent Pediatrics. In this amendment, we are responding to the labeling deficiencies communicated in the facsimile and the additional requests made by telephone.

As required by 21 CFR 314.94(D)(5), WE Pharmaceuticals, Inc. is forwarding a true copy of the amendment, including a completed copy of FDA form 356h. This additional amendment is submitted in (1) volume. WE Pharmaceuticals, Inc. is filing an archival copy (blue folder) and a technical review copy (red) of this submission.

The manufacturing facility for the finished product is Kiel laboratories, Inc., located at 2225 Centennial Dr., Gainesville, GA 30504. We certify that a true copy of this amendment has been provided to the Food and Drug Administration, Atlanta District office, Atlanta, GA.

Please direct any written communication regarding this ANDA to me at the above address. If you have any technical questions or require additional information, please feel free to contact H. Greg Thomas, Vice President, Kiel Laboratories, Inc., at (770) 534-0079.

Sincerely,

Craig H. Wheeler
President



Allergy/Asthma Products

P.O. Box 1142, Ramona, California 92065 • (760) 788-9155 • (800) 262-9555 • FAX (760) 788-9445 • <http://www.weez.com>

October 26, 2001

Mr. Gary Buehler
Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

N/FA

SUBJECT: TELEPHONE AMENDMENT TO ANDA 75-250
RE: Prednisolone Sodium Phosphate Oral Solution, 15mg/5mL

Dear Mr. Buehler,

Reference is made to a communication by telephone on October 23, 2001 regarding documentation for an outside testing laboratory used for _____ ANDA 75-250. In this amendment, we are including documentation stating that the testing performed by the facility operated by _____

As required by 21 CFR 314.94(D)(5), WE Pharmaceuticals, Inc. is forwarding a true copy of the amendment, including a completed copy of FDA form 356h. This additional amendment is submitted in (1) volume. WE Pharmaceuticals, Inc. is filing an archival copy (blue folder) and a technical review copy (red) of this submission.

The manufacturing facility for the finished product is Kiel laboratories, Inc., located at 2225 Centennial Dr., Gainesville, GA 30504. We certify that a true copy of this amendment has been provided to the Food and Drug Administration, Atlanta District office, Atlanta, GA.

Please direct any written communication regarding this ANDA to me at the above address. If you have any technical questions or require additional information, please feel free to contact H. Greg Thomas, Vice President, Kiel Laboratories, Inc., at (770) 534-0079.

Sincerely,

Craig H. Wheeler
President



Fax Cover Sheet



Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Rockville, Maryland

This document is intended only for the use of the party to whom it is addressed and may contain information that is privileged, confidential, and protected from disclosure under applicable law. If you are not the addressee, or a person authorized to deliver the document to the addressee, this communication is not authorized. If you have received this document in error, immediately notify us by telephone and return it to us at the above address by mail. Thank you.

To: Jeff Kiel
Fax: 770-534-0229

Phone: _____

From: Debra M. Catterson
Fax: 301-443-3847

Phone: 301-827-5846

Number of Pages (including cover sheet): 6

Date: 10/30/01

Comments:

See attached pages "14, 15, 17, 22, and 23"
for the requested revisions.

** Please be sure to make these revisions to the

labeling for BOTH applications: ANDA 75-181
and ANDA 75-250

Thanks!

Debbie Catterson

5 page/s of draft
labeling was/were
removed from this portion
of the ~~review~~

FDA FAX 10/30/2001



November 16, 2001

Mr. Gary Buehler
Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NIAP

DRUG AMENDMENT

**SUBJECT: FAXED AMENDMENT RESPONSE (Labeling)
ANDA 75-250**

RE: Prednisolone Sodium Phosphate Oral Solution, 15mg(base)/5mL

Dear Mr. Buehler,

Reference is made to your facsimile dated October 30, 2001 regarding labeling deficiencies for Prednisolone Sodium Phosphate Oral Solution, 15mg(base)/5mL, ANDA 75-250. In this amendment, we are responding to the labeling deficiencies communicated in the facsimile.

As required by 21 CFR 314.94(d)(5), Kiel Laboratories™ on behalf of WE Pharmaceuticals, Inc. is forwarding a true copy of the amendment, including a completed copy of FDA form 356h. This additional amendment is submitted in (1) volume. Kiel Laboratories™ on behalf of WE Pharmaceuticals, Inc. is filing an archival copy (blue folder) and a technical review copy (red) of this submission.

The manufacturing facility for the finished product is Kiel Laboratories™, located at 2225 Centennial Dr., Gainesville, GA 30504. Kiel Laboratories™ on behalf of WE Pharmaceuticals, Inc. certifies that a true copy of this amendment has been provided to the Food and Drug Administration, Atlanta District office, Atlanta, GA.

Please direct any written communication regarding this ANDA to me, H. Greg Thomas, Vice President, Kiel Laboratories™, at (770) 534-0079.

Sincerely,

H. Greg Thomas, Ph.D.
Vice President





NAI (patent)
WFS 3-11-02

Allergy/Asthma Products

P.O. Box 1142, Ramona, California 92065 • (760) 788-9155 • (800) 262-9555 • FAX (760) 788-9445 • <http://www.weez.com>

February 25, 2002

Mr. Gary Buehler
Director, Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

N/AM

ORIG AMENDMENT

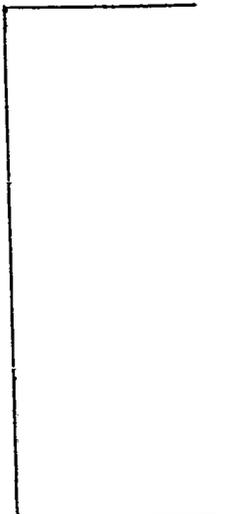
SUBJECT: MINOR AMENDMENT

**RE: Prednisolone Sodium Phosphate Oral Solution,
15mg(base)/5mL, ANDA 75-250**

Dear Mr. Buehler,

In this Minor Amendment, WE Pharmaceuticals, Inc. is submitting information regarding a Settlement and License Agreement, effective February 15, 2002 between WE Pharmaceuticals, Inc. and Celltech Pharmaceuticals, USA. Also, updated labeling, chemistry, manufacturing, and controls information is provided identifying any changes from the conditions under which the product was tentatively approved.

WE Pharmaceuticals, Inc. has been granted a non-exclusive license to make, use, offer to sell, or sell any product containing the formulation set forth in WE's ANDA No. 75-250 relating to the Prednisolone Sodium Phosphate Oral Solution for the 15mg/5mL strength from Celltech. A copy of the February 21, 2002 letter from Celltech to WE Pharmaceuticals, Inc. confirming the aforementioned agreement is included.

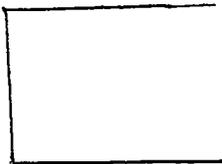


OK UNCL
d.
8 2002

CD RESEARCH

Handwritten signature and date: 3/5/02

Mr. Gary Buehler
February 25, 2002
Page 2



As required by 21 CFR 314.94(d)(5), WE Pharmaceuticals, Inc. is forwarding a true copy of this submission, including a completed copy of FDA form 356h. This information is submitted in (1) volume. WE Pharmaceuticals, Inc. is filing an archival copy (blue folder) and a technical review copy (red) of this submission. WE Pharmaceuticals, Inc. certifies that a true copy of this supplement has been provided to the Food and Drug Administration, Atlanta District office, Atlanta, GA.

Please direct any written communication regarding this ANDA to me at the above address. If you have any technical questions or require additional information, please feel free to contact H. Greg Thomas, Vice President, Kiel Laboratories™, at (770) 534-0079.

Sincerely,

A handwritten signature in cursive script that reads "Craig H. Wheeler".

Craig H. Wheeler
President

LAW OFFICES OF
THOMAS A. MAGLIOZZI
462 STEVENS AVENUE
SUITE 103
SOLANA BEACH, CALIFORNIA 92075
TELEPHONE: (858) 481-6001
FACSIMILE: (858) 481-6329

April 15, 2002

**BY FACSIMILE TO (301) 827-5911
AND FIRST-CLASS MAIL**

Mr. Peter Rickman
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

**Re: Prednisolone Sodium Phosphate Solution,
15mg(base)/5mL, ANDA 75-250**

Dear Mr. Rickman:

During our April 9, 2002 telephone discussion you recommended that WE Pharmaceuticals, Inc. contact Ruby Yu to arrange a direct dialogue on a "scientific level" between the Agency's chemist and a representative of Kiel Laboratories, Inc., WE's contract manufacturer.

Pursuant to your recommendation, a representative of Kiel Laboratories, Inc., did place a call to Ms. Yu for the purpose of setting up a teleconference with the Agency's chemist. It has now come to my attention that Ms. Yu has replied by leaving a voice mail message indicating that the requested teleconference would not be arranged.

I intend to respond more fully to this refusal after reviewing the details of the communications between Ms. Yu and Kiel Laboratories, Inc. In the meantime, please be advised that WE Pharmaceuticals, Inc. does not agree or acquiesce to classification of its pending amendment dated February 25, 2002 as a "major" amendment.

Very truly yours,



Thomas A. Magliozzi

RECEIVED

JUN 14 2002

cc: Craig H. Wheeler OGD / CDER