A Trusted Name For Over Half A Century

PUREPAC

ORIGINAL

Purepac Pharmaceutical Co.
200 Elmora Avenue, Elizabeth, New Jersey 07207
908-527-9100
Fax: 908-527-0649

Note: 2 cys
This is not
required
TA letter
also see 4/28/99
piece
M Anderson 5/13/99

UPS OVERNIGHT COURIER

March 30, 1999

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

MINOR AMENDMENT

Re: ANDA # 75-253, Ticlopidine Hydrochloride Tablets, 250 mg.

Dear Mr. Sporn,

Reference is made to Purepac Pharmaceutical Co.'s tentatively approved Abbreviated New Drug Application (ANDA) for Ticlopidine Hydrochloride (Ticlopidine HCl) Tablets USP, 250 mg and to a telephone conversation between Janak Jadeja of Purepac and Kassandra Sherrod of OGD on March 12, 1999. As directed by Ms. Sherrod, we are hereby providing a Minor Amendment to the above referenced ANDA to provide for the following alternate source of active pharmaceutical ingredient (API):

Ticlopidine HCl, USP

To support this amendment, Purepac has manufactured Ticlopidine HCl Tablets, 250 mg, Test Batch # PI-1033 containing API manufactured by ICFI. This test batch was derived from Master Formula # P-2613-2A which represents the same formulation and manufacturing process as the exhibit batch utilized in the Bioequivalence study.

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GENERIC DRUGS

In conjunction with this submission, Purepac is providing a Field Copy of this amendment to our local District Office in accordance with 21 CFR 314.71(b). Please note that the required Field Copy Certification is contained in Section 7 of this amendment. Please refer to the attached Table of Contents for a complete listing of information supporting this amendment.

If there are any questions concerning this submission, please contact the undersigned at (908) 659-2430. Purepac trusts that you will find this amendment complete and in order, and looks forward to your approval.

Sincerely,

PUREPAC PHARMACEUTICAL CO.

Joan Janulis, R.A.C.
Vice President, Regulatory Affairs

Enclosures

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200 Elmora Avenue, Elizabeth, New Jersey 07207
908-527-9100
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FACSIMILE AMENDMENT

UPS OVERNIGHT COURIER

March 11, 1998

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

RE: ANDA #75-253, Ticlopidine Hydrochloride Tablets, 250 mg

Dear Mr. Sporn:

Reference is made to our November 14, 1997 submission of an Abbreviated New Drug Application, ANDA #75-253 for Ticlopidine Hydrochloride Tablets, 250 mg. Further reference is made to your Facsimile Amendment dated March 6, 1998, requesting labeling revisions. Your comments are provided in bold type, followed by our response:

Labeling Deficiencies:

1. GENERAL COMMENTS:

Replace the "CAUTION: Federal law..." statement with the symbol "Rx only" or "℞ only". We refer you to the Guidance for Industry, "Implementation of Section 126, Elimination of Certain Labeling Requirements...", at the internet site, http://www.fda.gov/cder/guidance/index.htm for guidance.

Purepac's Response:

The required symbol has been incorporated into our final printed container labels and package insert.

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2. CONTAINER - 30s and 100s - Include the following statement in bold face type.

NOTE: It is essential that CBCs (including platelet count) and white cell differentials be performed every two weeks, starting at baseline before treatment is initiated to the end of the third month of therapy with ticlopidine hydrochloride (see accompanying insert).

Purepac's Response:

The final printed container labels were revised to include the above statement.

3. INSERT (specific comments are not provided in this letter).

Purepac's Response:

The final printed package insert was revised in accordance with your insert comments.

4. PATIENT PACKAGE INSERT (PPI)

a. (Specific revisions to the text are not provided in this letter.)

Purepac's Response:

The requested revisions have been incorporated into our patient package insert.

b. Please indicate where the PPI will be attached to the insert.

Purepac's Response:

One patient package insert is physically attached to each professional insert. The PPI is located at the bottom of the insert thus allowing the pharmacist to easily detach the PPI for patient use. Please refer to the final printed insert samples contained in this submission, which incorporate the PPI.

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c. Please comment on how (including the number of PPIs for the 100s size) the PPI will accompany with your package sizes.

Purepac's Response:

A single package insert, which contains a patient package insert, will be included in each product container of 30 and 100 units, at the time of packaging. For the 100 tablet container, two additional PPIs will be affixed to the top of the child resistant closure.

Please revise your labels and labeling, as instructed above, and submit 4 draft copies for a tentative approval or 12 final printed copies for a full approval of this application. If draft labeling is provided, please be advised that you will be required to submit 12 final printed copies of all labels and labeling at least 60 days prior to full approval of this application.
In addition, you should be aware that color and other factors (print size, prominence, etc) in final printed labeling could be found unacceptable and that further changes might be requested prior to approval.

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 enclosed, mocked up copy of your last submission with all differences annotated and explained.

Purepac's Response:

Purepac hereby submits twelve (12) final printed container labels for each package size (30s and 100s), twelve (12) final printed professional package inserts, and twelve (12) individual Patient Package Inserts (PPI's) in support of our request for final ANDA approval.

Also, enclosed please find comparisons of our original container labels and package insert and our newly revised labeling with all differences annotated and explained.

Please be advised that Purepac previously submitted Patent Amendments to this application on December 23, 1997 and February 6, 1998. The December 23 amendment addressed the requirements of 21 CFR 314.95(e) (documentation of receipt of notice by Patent/NDA holder). The February 6 amendment confirmed the absence of any legal action by the Patent/NDA holder within the 45 day period defined by statute.

Having completed submission of the above-referenced documentation, Purepac looks forward to the issuance of a final approval letter for this application.

This concludes our Facsimile Amendment in response to your correspondence dated March 6, 1998. If you have any questions regarding this submission, please do not hesitate to contact the undersigned at (908) 659-2430.

Sincerely,

PUREPAC PHARMACEUTICAL CO.

Joan Janulis, R.A.C.
Vice President, Regulatory Affairs

JJ:cch

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Purepac Pharmaceutical Co.
200 Elmora Avenue, Elizabeth, New Jersey 07207
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PATENT AMENDMENT

UPS OVERNIGHT COURIER

December 23, 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

RE: ANDA #75-253, Ticlopidine Hydrochloride Tablets, 250 mg

Dear Mr. Sporn:

Reference is made to our November 14, 1997 submission of an Abbreviated New Drug Application, ANDA #75-253 for Ticlopidine Hydrochloride Tablets, 250 mg. Further reference is made to our December 16, 1997 amendment in accordance with 21 CFR 314.95(b) in which Purepac certified that Syntex Laboratories, Inc., owner of U.S. patent #4,591,592 and the holder of the approved application for the listed drug, was sent notice of patent certification.

As required by 21 CFR 314.95(e), Purepac Pharmaceutical Co. is providing, as documentation of receipt of notice, a copy of the certified mail return receipt from Syntex Laboratories, Inc. which is dated December 19, 1997.

If there are any questions concerning this amendment, please contact the undersigned at (908) 659-2430.

Sincerely,

PUREPAC PHARMACEUTICAL CO.

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GENERIC DRUGS

Joan Janulis, R.A.C.
Vice President, Regulatory Affairs

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Purepac Pharmaceutical Co.
200 Elmora Avenue, Elizabeth, New Jersey 07207
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Fax: 908-527-0649

NEW CORRESP
NC

Called Doug Sporn's office on 12/23/97 to remind her that she needs to provide us with a copy of the return receipt to show proof of notification.
12/23/97

PATENT AMENDMENT

UPS OVERNIGHT COURIER

December 16, 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

RE: ANDA #75-253, Ticlopidine Hydrochloride Tablets, 250 mg

Dear Mr. Sporn:

Reference is made to our November 14, 1997 submission of an Abbreviated New Drug Application, ANDA #75-253 for Ticlopidine Hydrochloride Tablets, 250 mg. Further reference is made to your December 11, 1997 letter (received by Purepac on December 15, 1997) acknowledging the receipt of this application.

In accordance with 21 CFR 314.95(b), Purepac Pharmaceutical Co. is amending the subject application to certify that the requirements stated in 21 CFR 314.95(a) and 21 CFR 314.95(c) have been satisfied. On December 15, 1997 a notice was sent to the holder of U.S. Patent 4,591,592 (the subject of our paragraph IV certification) and the holder of the approved application for the listed drug product Ticlid®. In this case, the patent holder and application holder are the same entity, i.e. Syntex Laboratories, Inc. The content of the notification sent to Syntex Laboratories, Inc. complied with the requirements set forth in 21 CFR 314.95(c).

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Purepac will further amend the application to provide documentation regarding the receipt of notice by Syntex Laboratories, inc. as it becomes available.

If there are any questions concerning this amendment, please contact the undersigned at (908) 659-2430.

Sincerely,

PUREPAC PHARMACEUTICAL CO.

Joan Janulis, R.A.C.
Vice President, Regulatory Affairs

JJ:cch

ANDA 75-253

Purepac Pharmaceutical Co.
Attention: Joan Janulis
200 Elmora Avenue
Elizabeth, New Jersey 07207

Dear Madam:

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: Ticlopidine Hydrochloride Tablets, 250 mg

DATE OF APPLICATION: NOVEMBER 14, 1997

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 17, 1997

You have filed a Paragraph IV patent certification in accordance with 21 CFR 314.94(a)(12)(I)(A)(4) and Section 505(j)(2)(A)(vii)(IV) of the Act. Please be aware that you need to comply with the notice requirements, as outlined below. In order to facilitate approval of this application, we suggest that you follow the outlined procedures below:

CONTENTS OF THE NOTICE

You must cite section 505(j)(2)(B)(ii) of the Act in the notice and should include, but not be limited to, the information as described in 21 CFR 314.95(c).

SENDING THE NOTICE

In accordance with 21 CFR 314.95(a):

- Send notice by **U.S.** registered or certified **mail** with return receipt requested to each of the following:

  1) Each owner of the patent or the representative designated by the owner to receive the notice;

2) The holder of the approved application under section 505(b) of the Act for the listed drug claimed by the patent and for which the applicant is seeking approval.

3) An applicant may rely on another form of documentation only if FDA has agreed to such documentation in advance.

DOCUMENTATION OF RECEIPT OF NOTICE

You must submit an amendment to this application that is plainly marked on the cover sheet "PATENT AMENDMENT" with the following:

- In accordance with 21 CFR 314.95(b), provide a statement certifying that the notice has been provided to each person identified under 314.95(a) and that notice met the content requirements under 314.95(c).

- In accordance with 21 CFR 314.95(e), provide documentation of receipt of notice by providing a copy of the return receipt or a letter acknowledging receipt by each person provided the notice.

- A designation on the exterior of the envelope and above the body of the cover letter should clearly state "PATENT AMENDMENT". This amendment should be submitted to your application as soon as documentation of receipt by the patent owner and patent holder is received.

DOCUMENTATION OF LITIGATION/SETTLEMENT OUTCOME

You must submit an amendment to this application that is plainly marked on the cover sheet "PATENT AMENDMENT" with the following:

- If litigation occurs within the 45-day period as provided for in section 505(j)(4)(B)(iii) of the Act, we ask that you provide a copy of the pertinent notification.

- Although 21 CFR 314.95(f) states that the FDA will presume the notice to be complete and sufficient, we ask that if you are not sued within the 45-day period, that you provide a letter immediately after the 45 day period elapses, stating that no legal action was taken by each person provided notice.

- You must submit a copy of a final order or judgement from which no appeal may be taken (which might not be the one from the District Court), or a settlement agreement

between the parties, whichever is applicable, or a licensing agreement between you and the patent holder, or any other relevant information. We ask that this information be submitted promptly to the application.

If you have further questions you may contact Peter Rickman, Chief Regulatory Support Branch, at (301)827-5862.

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

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

Should you have questions concerning this application, contact:

Kassandra Sherrod
Project Manager
(301) 827-5849

Sincerely yours,

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

cc: ANDA 75-253

Endorsements:
HFD-615/P.Rickman, Chief PSB/ /S/ 9/97
HFD-615/N.Mahmud/PM/
x:\new\firmnz\purepac\ltrs&rev\75253.ack
FT/
ANDA Acknowledgment Letter!

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PUREPAC

Purepac Pharmaceutical Co.
200 Elmora Avenue, Elizabeth, New Jersey 07207
908-527-9100
Fax: 908-527-0649

UPS OVERNIGHT COURIER

November 14, 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

RE: Abbreviated New Drug Application for Ticlopidine Hydrochloride Tablets, 250 mg

Dear Mr. Sporn,

In accordance with the regulations promulgated under Section 505(j) of the Federal Food, Drug and Cosmetic Act as amended, Purepac Pharmaceutical Co. is submitting this Abbreviated New Drug Application (Archival and Review Copies) for Ticlopidine Hydrochloride Tablets, 250 mg.

This Abbreviated New Drug Application has been prepared in accordance with Policy and Procedure Guide #30-91, dated April 10, 1991, and contains a total of 15 volumes comprising the Archival Copy and the Review Copy (chemistry, manufacturing and controls review part and bioavailability/ bioequivalence review part).

In conjunction with this submission, Purepac has provided a Field Copy of this application to our local district office in accordance with 21 CFR 314.94(d)(5). Please note that the required Field Copy Certification is contained in Section XXI of our abbreviated application.

In addition, a certification in accordance with Section 306(K) of the Federal Food Drug and Cosmetic Act as amended by the "Generic Drug Enforcement Act" is contained in Section IX of this application. Three (3) separately bound copies of the analytical methods and related descriptive information are also included.

Regarding the packaging of the primary exhibit batch supporting this application, Purepac partially packaged the batch without a previously approved protocol in accordance with Policy and Procedure Guide #41-95 Section E(2). The uniformity data and sampling protocol required by the guidance is contained in Section XII of our application.

Since Ticlopidine Hydrochloride raw material and Ticlopidine Hydrochloride Tablets are not the subjects of monographs in USP, Purepac has developed in-house test methods for the analysis of the active drug substance, in-process blend, finished product and stability samples. Purepac acknowledges that the analytical methods for the active drug substance and drug product will be validated by an FDA laboratory. The appropriate samples are available upon FDA request.

Purepac acknowledges that all firms referenced in this ANDA, with respect to the manufacture and testing of the subject drug product, must be in compliance with current good manufacturing practices at the time of approval. A signed acknowledgment is contained in Section IX of this application. Additionally, Purepac acknowledges that all DMFs referenced in this ANDA have to be found satisfactory at the time of approval of the ANDA.

Purepac Pharmaceutical Co. trusts that you will find this application complete and well organized, and looks forward to the review process. If you have any questions concerning this submission, please do not hesitate to contact me at telephone number (908) 527-9100 extension 2430, or fax number (908) 659-2440.

Sincerely,

PUREPAC PHARMACEUTICAL CO.

Joan Janulis, R.A.C.
Vice President, Regulatory Affairs

JJ:cch
Enclosures