CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75161

ADMINISTRATIVE DOCUMENTS

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

ANDA Number: 75-161 Date of Submission: July 8, 1997

Applicant's Name: Genpharm Inc.

Established Name: Ticlopidine Hydrochloride Tablets, 250 mg

Labeling Deficiencies:

1. CONTAINER - 30's, 100's, & 500's

   a. 30's & 100's

      Satisfactory in draft

   b. 500's - 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).

2. CARTON

   a. 30's & 100's

      i. Revise to read "Store at controlled room temperature 15° - 30°C (59° - 86°F).

      ii. Revise to read "NOTE: It is ... of therapy with ticlopidine hydrochloride (See accompanying insert)". [add "with ticlopidine hydrochloride"]

   b. 98 tablets (Unit Dose) - Include the following statements on the carton:

      USUAL DOSAGE: One tablet two times a day with meals. See package insert for full prescribing information.

NOTE TO DISPENSER: Please provide a patient package insert when the blister pack is dispensed.

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).

3. UNIT DOSE BLISTER

Satisfactory in draft

4. INSERT

a. DESCRIPTION - Revise the third paragraph to read as follows:

i. Each tablet, for oral administration, contains 250 mg of ticlopidine hydrochloride. In addition, each tablet contains the following inactive ingredients: ammonium ... triacetin. [You may delete the last sentence "The tablets ... side"]

ii. Please include the botanical source for starch [e.g. starch (corn)].

b. CLINICAL PHARMACOLOGY (Pharmacokinetics and Metabolism)

Relocate the fifth paragraph to be the last sentence of the fourth paragraph.

c. INDICATIONS AND USAGE - First sentence:

Ticlopidine hydrochloride tablets are ...

d. ADVERSE REACTIONS - Table:

i. Please italicize the numbers of the first row to be consistent with the innovator's.

ii. Legend of the table:

Incidence of discontinuation, regardless of relationship to therapy, ... [add "to"]

e. DOSAGE AND ADMINISTRATION

The recommended dose of ticlopidine hydrochloride tablets is ... [add "tablets"]

f. HOW SUPPLIED

i. Add "biconvex" to the description of your drug product.

ii. Add "unscored" to the description of your drug product.

iii. Include "Dispense in" statement as appears on the container labels.

iv. Revise the storage recommendations to read "Store at controlled room temperature 15° - 30°C (59° - 86°F)".

v. We encourage you to include the legend "Caution: Federal law ....".

h. IMPORTANT INFORMATION ABOUT TICLOPIDINE HCL Tablets

Third paragraph, third sentence:

... ticlopidine hydrochloride (about 1%) develop ... [Note: This change is based on the last approved innovator's labeling]

5. PATIENT PACKAGE INSERT (PPI)

i. Refer to the comment (h) under INSERT.

ii. Please comment on the number of PPIs and how they will be supplied with each container size including Unit Dose carton.

Please revise your labels and labeling, as instructed above, and submit in final print. Alternatively, you may submit printers proof for the patient package insert and professional insert labeling if your prefer. Please note that the final printed insert labeling is not required for tentative approval of an application if it is granted with more than 90 days remaining from the date when full approval can be considered.

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 explained.

/S/

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

3.1

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

ANDA Number: **75-161** Date of Submission: **September 22, 1998**

Applicant's Name: **Genpharm Inc.**

Established Name: **Ticlopidine Hydrochloride Tablets, 250 mg**

Labeling Deficiencies:

INSERT

a. DESCRIPTION

We note that you have changed the listing of inactive ingredients from the one appearing in the insert labeling submitted April 2, 1998. It appears that the listing is the same as the listing appearing in the innovator's labeling. Please revise and/or comment. If you have changed the components of your drug product to be the same as Ticlid®, please submit the updated Components and Composition statements.

b. INDICATIONS AND USAGE - Second paragraph:

... purpura (TTP) and... [rather than "TPP"]

c. HOW SUPPLIED

a. We note that the imprinting information on your drug product is different from the one appearing in the insert submitted April 2, 1998 (*i.e.*, changed to "printed in blue" from "debossed"). Please revise and/or comment.

b. We encourage the relocation of "Rx Only" statement to the TITLE section.

Please revise package insert labeling as instructed above, and submit 12 final printed copies for a full approval of this application.

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 explained.

Jerry Phillips
Director
Division of Labeling and Program Support
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: **75-161** Date of Submission: **April 2, 1998**

Applicant's Name: **Genpharm Inc.**

Established Name: **Ticlopidine Hydrochloride Tablets, 250 mg**

Labeling Deficiencies:

INSERT

Due to significant changes throughout the labeling of the listed drug, please revise your labeling to be in accord with the attached labeling of the listed drug (Ticlid® Tablets - Roche Hexagon; Revised June 1998, Approved July 15, 1998).

Please revise labeling as instructed above, and submit 12 final printed copies for a full approval of this application.

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 explained.

/S/ for

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

Attached: Copy Of Approved Ticlid® Labeling

LABEL DEFICIENCY LETTER
Dated August 11, 1998

Attached in the following pages is the letter received, August 11, 1998 from Mr. Jerry Phillips concerning labeling deficiencies for Ticlopidine ANDA 75-161.

In a telephone conversation (September 15, 1998) with Mr. Philips, he requested that Genpharm provide updated final print copies of the Patient Package Insert (PPI), in addition to the information requested in the August 11, 1998 letter. Mr. Philips also requested that Genpharm indicate the number of Patient Package Inserts which would accompany each package to the Pharmacists for distribution to patients.

In our Major Amendment response (letter dated November 6, 1997) we indicated that a pad of 5 PPI's will be enclosed with each shipment. The number of pads provided will be based on the following distributions:

Bottle of 500	2 pads will be provided
Bottle of 100	1 pad will be provided
Bottle of 30	1 pad will be provided
Blister carton of 98	1 pad will be provided