CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
21-268

Approval Letter

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-268

NOV 1 2001

Unimed Pharmaceuticals, Inc.
Attention: Ms. Judy Athey
Four Parkway North
Suite 200
Deerfield, IL 60015-2544

Dear Ms. Athey:

Please refer to your new drug application (NDA) dated August 30, 2000, received August 30, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Teveten HCT (eprosartan mesylate/hydrochlorothiazide) Tablets.

We acknowledge receipt of your submissions dated July 5 and 18 (two), September 6 and 28, 2001. Your submission of September 28, 2001 constituted a complete response to our June 27, 2001 action letter.

This new drug application provides for the use of Teveten HCT (eprosartan mesylate/hydrochlorothiazide) Tablets for hypertension.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text and with the minor editorial revisions listed below. Accordingly, the application is approved effective on the date of this letter.

1. The positions of the double bonds in the imidazole ring of the eprosartan mesylate structure have been corrected in the package insert.

2. Under **DOSAGE AND ADMINISTRATION/Replacement Therapy**, the following paragraph has been added:

   > If the patient under treatment with Teveten® HCT requires additional blood pressure control at trough, or to maintain a twice a day dosing schedule of monotherapy, 300 mg TEVETEN® may be added as evening dose.

3. In the table under the **HOW SUPPLIED** section, we recommend that the complete NDC code be placed in the appropriate column at the time of your next printing, as follows:

Eprosartan (mg)	HCTZ (mg)	Color	NDC
600	12.5	Butterscotch	NDC 0051-5147-01
600	25	Brick red	NDC 0051-5150-01

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the submitted draft labeling (package insert submitted September 28, 2001). These revisions are terms of the NDA approval. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-268." Approval of this submission by FDA is not required before the labeling is used.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We are waiving the pediatric study requirement for this action on this application.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Ms. Sandra Birdsong
Regulatory Project Manager
(301) 594-5334

Sincerely,

/S/

{See appended electronic signature page}

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

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JUN 27 2001

Unimed Pharmaceuticals, Inc.
Attention: Ms. Judy Athey
Four Parkway North
Deerfield, IL 60015-2544

Dear Ms. Athey:

Please refer to your new drug application (NDA) dated August 30, 2000, received August 30, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Teveten HCT (eprosartan mesylate/hydrochlorothiazide) 600/12.5 and 600/25 mg Tablets.

We acknowledge receipt of your submissions dated October 5 and 19, November 2 and 9, and December 19, 2000, March 23, April 19 and 30, May 2 and 15, June 20 and 22, 2001.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit the final printed labeling (FPL) revised as indicated in the enclosed marked-up draft. In addition, please make the following changes:

1. The positions of the double bonds in the imidazole ring of the eprosartan mesylate structure should be corrected in the package insert.

2. All container labels should be revised as follows:

   a) the strength should not appear on the same line as the established or generic names.

   b) the strength of 600 mg should be modified with an asterisk (600*) on the same line after the trade name or on a separate line after the trade name or established names. The asterisk is to be used for a note on the label to state that each tablet contains 735.8 mg of eprosartan mesylate, equivalent to 600 mg of eprosartan, with 12.5 or 25 mg of hydrochlorothiazide, as appropriate. An example is given below:

TEVETEN HCT
(eprosartan mesylate/hydrochlorothiazide)
600* mg/12.5 mg
*Each tablet contains 735.8 mg of eprosartan mesylate
equivalent to 600 mg of eprosartan and 12.5 mg of hydrochlorothiazide

3. To support the option of once or twice daily dosing, the tablets should be scored.

Based on the stability data, an expiration date of two years is granted for the 600/12.5 mg Tablets.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL, ten of which individually mounted on heavy weight paper or similar material.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, please contact:

Ms. Sandra Birdsong
Regulatory Health Project Manager
(301) 594-5334

Sincerely,

/S/

{See appended electronic signature page}

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

17 pages redacted from this section of the approval package consisted of draft labeling