CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-120

APPROVAL LETTER

NDA 20-120

Muro Pharmaceuticals, Inc
890 East Street
Tewksbury, Massachusetts 01876-1496

Attention: Joseph Celona
Director of Regulatory Affairs

Dear Mr. Celona:

Please refer to your new drug application (NDA) dated April 27, 1992, received April 28, 1992, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Tri-Nasal (triamcinolone acetonide) Nasal Spray.

We acknowledge receipt of your submissions dated May 20, and September 8, 1992, October 31, 1995, February 12, and 15, March 7, April 1, 9, 11, 24, and 29, May 7, June 4, July 1, 22, and 24, and August 2, 1996, April 14, and November 24, 1997, March 13, 1998, July 22, October 14, and 29, and November 22, 1999, January 20, and 31, and February 3, 2000. Your submission of July 22, 1999, constituted a complete response to our April 20, 1998, action letter.

This new drug application provides for the use of Tri-Nasal (triamcinolone acetonide) Nasal Spray for the treatment of nasal symptoms of seasonal and perennial allergic rhinitis in adults and children 12 years of age or older.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert, patient package insert, immediate container and carton labels submitted February 3, 2000). 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 20 copies of the FPL as soon as it is available, in no case 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 20-120." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submission dated January 19, 2000. These commitments, along with any completion dates agreed upon, are listed below.

1. You committed to conduct a well-controlled, prospective growth study of the effects of Tri-Nasal Spray on growth in prepubertal children. The results of this study should be reported to the Agency by January 24, 2003. You will consult the Division regarding the design and conduct of such a trial.

2. You committed to [ ]. Status reports will be submitted to FDA in a special post market report as per 21 CFR 314.81(b)(3)(vii) within 3 months of approval of the NDA.

3. You committed to conduct two in-vitro genotoxicity studies with triamcinolone acetonide-21-aldehyde and submit the results within six months of approval of the NDA.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

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-40
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, call Mrs. Sandy Barnes, Project Manager, at (301) 827-1075.

Sincerely,

Robert J. Meyer, M.D.
Director
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-120

APPROVABLE LETTER

Food and Drug Administration
Rockville MD 20857

NDA 20-120

APR 20 1998

Muro Pharmaceutical, Inc.
890 East Street
Tewksbury, Massachusetts, 01876-1496

Attention: Joseph Celona
Director of Regulatory Affairs

Dear Mr. Celona:

Please refer to your April 27, 1992, new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tri-Nasal Spray (triamcinolone acetonide nasal solution, 50 mcg).

We acknowledge receipt of your submissions dated November 24, 1997, and March 13, 1998.

This application provides for the treatment of the nasal symptoms of seasonal and perennial allergic rhinitis in adults and children 12 years of age and older.

We have completed the review of this application as submitted with draft labeling, and it is approvable. Before this application may be approved, however, it will be necessary for you to provide the information requested below.

1. Provide complete analytical data for all attributes or Certificates of Analysis on all batches of _____ received from _____

WITHHOLD 5 PAGE (S)

17. Comments on acceptance criteria and test procedures, discussed in this letter, will be deferred until all related issues are resolved. All revised test procedures and acceptance criteria should be submitted.

18. We have the following preliminary comments regarding labeling. Please submit draft labeling incorporating the revisions below and the revisions shown on the enclosed revised package insert and patient instructions for use.

    a. The batch number and the expiration date should be included on the bottle labeling.

    b. If space allows, priming information should be included on the bottle labeling. If not, it should be added to the package label.

    c. The established name on the bottle label is at least half of the trade name, however it should be in bold print.

    d. The comment regarding ———— should be removed from the carton label.

e. Item 4 in the directions for use section of the Patients Instructions for Use, directs the patient to [redacted] This is not consistent with other corticosteroid nasal sprays. Provide an explanation for this difference. Also, provide the specific instructions for use which were given to patients in studies 100-305 and 100-309.

Additional labeling comments will be forwarded following satisfactory resolution of the above items.

You are advised to contact the division regarding the extent and format of your safety update prior to responding to this letter.

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 such action FDA may take action 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.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal or telephone conference with the Division to discuss what further steps need to be taken before the application may be approved. You are strongly encouraged to request a meeting with the Division to discuss the deficiencies noted in this letter prior to submitting your response.

The drug 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. Sandy Barnes, Project Manager, at (301) 827-1075.

Sincerely yours,

/S/

John K. Jenkins, M.D., F.C.C.P.
Director
Division of Pulmonary Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

WITHHOLD 41 PAGE (S)

Draft

Labeling

Barr

NDA 20-120

OCT 8 1997

Muro Pharmaceutical, Inc.
890 East Street
Tewksbury, Massachusetts 01876-1496

Attention: Joseph A. Celona
Director of Regulatory Affairs

Dear Mr. Celona:

Please refer to your new drug application dated April 27, 1992, received April 28, 1992, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tri-Nasal Spray (triamcinolone acetonide nasal spray, 50 mcg).

We acknowledge receipt of your submission dated April 14, 1997.

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 information requested below.

1. Provide data which support the use of [redacted] This information should include impurity profiles from comparative accelerated stability data for drug product manufactured with [redacted] material.

2. DMF [redacted] has been reviewed and has been found to be inadequate to support this application. A letter dated September 3, 1997 was sent to the holder.

3. The following comments pertain to the Raw Material Specification for triamcinolone acetonide.

[redacted]

The following comments pertain to the drug product.

4. An updated master batch record should be submitted to reflect the following:

WITHHOLD 7 PAGE (S)

Due to the July 29, 1997 Federal Register Notice on environmental assessment, we recommend that you submit a request for a categorical exclusion in accordance with 21 CFR 25.31(b).

Further labeling comments, in addition to those forwarded to you in our September 17, 1996 Not Approvable letter, will be forwarded following satisfactory resolution of the above comments.

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 such action FDA may take action to withdraw the application.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal or telephone conference with the Division to discuss what further steps need to be taken before the application may be approved.

The drug 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. Sandy Barnes, Project Manager, at (301) 827-1075.

Sincerely yours,

John K. Jenkins, M.D., F.C.C.P.
Director
Division of Pulmonary Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

cc:

Original NDA 20-120
HFD-570/Div. Files
HFD-002/ORM
HFD-92/DDM-DIAB
HFD-570/S.Barnes
HFD-570/L. Ng
HFD-570/Nicklas
HFD-570/Whitehurst
HFD-570/Gillespie
HFD-570/Gebert
DISTRICT OFFICE
HFD-40/DDMAC (with draft labeling)

Drafted by: S. Barnes
/September 30, 1997/WORD PERFECT N:N20120.AE
Initialed by: C. Schumaker 10/4/97
L. Ng 10/6/97
G. Poochikian 10/6/97 /S/ 10/8/97
V. Whitehurst 10/6/97 /S/
H. Sheevers 10/6/97
B. Gillespie 10/6/97 10/8/97
D. Conner 10/6/97 /S/ 10/8/97
R. Nicklas 10/7/97 /S/ 10/8/97
P. Honig 10/7/97 /S/ 10/8/97
Final: P. Wilson 10/8/97 /S/ 10/9/97

APPROVABLE (AE)