CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-642

APPROVAL LETTER(S)

AP
01/31/05

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-642

Nastech Pharmaceutical Company, Inc.
Attention: Gordon Brandt, MD
Executive Vice President of Science and Clinical Development
3450 Monte Villa Parkway
Bothell, WA 98027

Dear Dr. Brandt:

Please refer to your new drug application (NDA) dated December 26, 2003, received December 29, 2003, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Nascobal (cyancobalamin, USP) Nasal Spray for intranasal administration.

We acknowledge receipt of your submissions dated November 3, 12, and 28, and December 1, 2004, and January 20, 2005.

The December 1, 2004, submission constituted a complete response to our October 28, 2004, action letter.

This new drug application provides for the use of Nascobal (cyanocobalamin) Nasal Spray for maintenance of normal hematologic status in pernicious anemia patients.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (package insert submitted January 20, 2005, and the immediate container and carton labels submitted December 1, 2004). 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 an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. 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. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-642**." Approval of this submission by FDA is not required before the labeling is used.

faxed copy
received - confirmed
by Steve in Wash.
Tue @ 935/am
2-1-05

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. We note that you have fulfilled the pediatric study requirement for this application.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send 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, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Holly Wieland, Regulatory Project Manager at (301) 827-6410.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-642

APPROVABLE LETTER(S)

AE 10/28/04

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-642

Nastech Pharmaceutical Company, Inc.
Attention: Gordon Brandt, MD
Executive Vice President of Science and Clinical Development
45 Davids Drive
Hauppauge, NY 11788

Dear Dr. Brandt:
Please refer to your new drug application (NDA) dated December 26, 2003, received December 29, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nascobal (cyanocobalamin nasal spray) 500 mcg/0.1 mL.

We acknowledge receipt of your submissions dated January 15 and 27, March 15, 22, and 24, August 31, September 10, 16, and 17, and October 8(2) and 13, 2004.

We completed our review of this application, as amended, and it is approvable. Before the application may be approved the following issues must be addressed:

1. Our field investigator could not complete inspection of the drug substance manufacturing facility at — ecause the facility was not ready for inspection. Satisfactory inspection is required before this application may be approved. Your complete response should indicate that an inspection has been completed.

2. After correcting for baseline values, the intranasal spray was 10% less bioavailable than the intranasal gel. This product is also less bioavailable than the intramuscular formulation. Since this product cannot be considered bioequivalent to the reference listed product, clinical use of this product or any cyanocobalamin formulation will require close monitoring of vitamin B_{12} levels. Patients not achieving adequate vitamin B_{12} levels will require increased dosing with subsequent blood monitoring.

    - Revise your package insert (PI) to include a discussion of the difference in pharmacokinetics of the two intranasal products and advice that patients treated with the nasal spray should have vitamin B_{12} levels closely monitored with dose amount and/or frequency adjusted to achieve adequate levels.

      Submit the revised draft labeling in your complete response. To facilitate our review, provide highlighted or marked up labeling. We are deferring additional comments on the PI labeling until we have received your response.

3. Change "room temperature" to "controlled room temperature" on the carton and container labels.

4. Regulatory Issues:

    - Submit Form FDA 3542a entitled "Patent Information Submitted With the Filing of an NDA, Amendment, or Supplement."

    - Clarify whether you are a full or partial assignee for patent #4,724,231.

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

In addition, you must submit the content of labeling in electronic format as described in 21 CFR 314.50(l)(5). Current guidance for industry specifies that the content of labeling should be provided in PDF or SPL file format. This new submission requirement was published on December 11, 2003 (68 FR 69009) and was effective June 8, 2004. For additional information, consult the following guidance for industry: *Regulatory Submissions in Electronic Format – Content of Labeling* (February 2004).

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. 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), you may request an informal meeting or telephone conference with this division to discuss what steps need to be taken before the application may be approved.

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, call Holly Wieland, Regulatory Project Manager, at (301) 827-6410.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Mary Parks
10/28/04 03:19:29 PM
for Dr. Orloff