DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-727

NitroMed, Inc.
Attention: Michael Sabolinski, M.D.
Senior VP, Clinical Development & Regulatory Affairs
125 Spring Street
Lexington, MA 02421

Dear Dr. Sabolinski:

Please refer to your new drug application (NDA) originally submitted July 3, 1996, under section 505(b) of the Federal Food, Drug, and Cosmetic Act for BiDil® (isosorbide dinitrate and hydralazine hydrochloride) Tablets, 20 mg/37.5 mg.

We acknowledge receipt of your submissions dated December 21, 2004 and January 4, 7, and 19, March 22, April 11, 15, 22, 25, 26, 27, and 29, May 6 and 9, and June 9, 10, and 23, 2005.

Your submission of December 21, 2004 constituted a complete response to our July 2, 1997 not approvable letter.

This new drug application provides for the use of BiDil® (isosorbide dinitrate and hydralazine hydrochloride) Tablets, 20 mg/37.5 mg for the treatment of heart failure as an adjunct to standard therapy in self-identified black patients to improve survival, to prolong time to hospitalization for heart failure, and to improve patient-reported functional status.

We have 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 in content to the enclosed labeling (text for the package insert) and the immediate container labels submitted on June 9, 2005. 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 20-727**." Approval of this submission by FDA is not required before the labeling is used.

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 refer you to our May 25, 2005 letter waiving the pediatric study requirement for this application.

Please continue to monitor the (b)(4) ---------- as an impurity/degradant in the release and stability testing of BiDil® tablets with a release/shelf life limit of not more than (NMT) (b)(4) Based on the stability data submitted, an expiration dating period of 6 months is assigned to BiDil® tablets when stored at 25°C.

We remind you of your commitments provided in the June 9, 2005 submission to:

1) submit a second identification test for inclusion in the drug product specifications by July 31, 2005

2) complete work on identification of impurity/degradation products in BiDil® tablets with revised specifications, if appropriate, by August 31, 2005.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

The following dissolution method and specification for both isosorbide dinitrate and hydralazine hydrochloride are recommended:

1) USP Apparatus I at (b)(4) PM in (b)(4) l of (b)(4) N HCl

2) Specification not less than (b)(4) in 30 minutes

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 one copy to the Division of Cardio-Renal Drug Products 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, 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, please call:

Dianne Paraoan
Regulatory Project Manager
(301) 594-5308

Sincerely,

{See appended electronic signature page}

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

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

/s/

Robert Temple

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