DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-705 S-015

First Horizon Pharmaceutical Corporation
Attention: Jennifer Schwartz
6195 Shiloh Road
Alpharetta, GA 30005

Dear Ms. Schwartz:

Please refer to your supplemental new drug application dated October 28, 2005, received October 31, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nitrolingual® Pumpspray (glyceryl trinitrate) 0.4 mg per spray.

This supplemental new drug application provides for instructions about dosage and administration that is intended to increase the safe use of the drug product. Specifically, this updated labeling incorporated new priming instructions to the patient in the event the product has not been used for longer than 6 weeks and modified the analytical procedure for Content Uniformity.

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 and with the minor editorial revisions listed below.

1. Under **How to Use Nitrolingual® Pumpspray**, the following was added to this section:

   Before using this product for the first time, the pump must be sprayed 5 times into the air (this is known as priming). The pump should be primed every 6 weeks to remain ready for use. If the product has not been used for 6 weeks, a prime of 1 spray is necessary.

2. Under NOTE, the 1st sentence has been revised from:

   When using this product for the first time or while priming the container, familiarize yourself with it by actuating the spray into the air (away from yourself and others).

   to

   To familiarize yourself with the product and while priming the container, actuate the spray into the air (away from yourself and others).

3. Under **Dosage**, the 2nd paragraph has been revised from:

   There are approximately 60 or 200 metered sprays of nitroglycerin per Nitrolingual® Pumpspray bottle (including all necessary primes). However, the number of times the medication may be used is dependent on the number of sprays per use (1 or 2 sprays), and frequency of repriming. Each metered spray of Nitrolingual® Pumpspray delivers 400 mcg of nitroglycerin after an initial priming of 1 spray. The container will remain adequately primed for 6 weeks. If the medication is not used within 6 weeks, it can be adequately reprimed with 1 spray.

   to

There are approximately 60 or 200 metered sprays of nitroglycerin per Nitrolingual® Pumpspray bottle. However, the number of times the medication may be used is dependent on the number of sprays per use (1 or 2 sprays), and frequency of repriming. Each metered spray of Nitrolingual® Pumpspray delivers 400 mcg of nitroglycerin after an initial priming of 5 sprays. The container will remain adequately primed for 6 weeks. If the medication is not used within 6 weeks, it can be adequately reprimed with 1 spray. Longer storage periods without use may require up to 5 repriming sprays.

4. Under **Precaution**, a new sentence has been added after the following sentence:

   The end of the pump should be covered by the fluid level.

   to

   The end of the pump should be covered by the fluid level. Once fluid falls below the level of the center tube, sprays will not be adequate and the container should be replaced.

5. In the **DOSAGE AND ADMINISTRATION** section, the 2nd paragraph has been revised and a new 3rd paragraph has been added:

   Each metered spray of Nitrolingual® Pumpspray delivers 48 mg of solution containing 400 mcg of nitroglycerin after an initial priming of 1 spray. It will remain adequately primed for 6 weeks. If the product is not used within 6 weeks it can be adequately reprimed with 1 spray. There are 60 or 200 metered sprays per bottle. The total number of available doses is dependent, however, on the number of sprays per use (1 or 2 sprays), and the frequency of repriming.

   to

   Each metered spray of Nitrolingual® Pumpspray delivers 48 mg of solution containing 400 mcg of nitroglycerin after an initial priming of 5 sprays. It will remain adequately primed for 6 weeks. If the product is not used within 6 weeks it can be adequately reprimed with 1 spray. Longer storage periods without use may require up to 5 repriming sprays. There are 60 or 200 metered sprays per bottle. The total number of available doses is dependent, however, on the number of sprays per use (1 or 2 sprays), and the frequency of repriming.

   The transparent container can be used for continuous monitoring of the consumption. **The end of the pump should be covered by the fluid level**. Once fluid falls below the level of the center tube, sprays will not be adequate and the container should be replaced. As with all other sprays, there is a residual volume of fluid at the bottom of the bottle which cannot be used.

6. In the **HOW SUPPLIED** section, the last sentence was revised from:

   Each unit contains 4.9 g (NDC 59630- 300-65) or 12 g (NDC 59630-300-20) (Net Content) of nitroglycerin lingual spray which will deliver 60 or 200 metered sprays containing 400 mcgs of nitroglycerin per spray.

   to

   Each unit contains 4.9 g (NDC 59630- 300-65) or 12 g (NDC 59630-300-20) (Net Content) of nitroglycerin lingual spray which will deliver 400 mcgs of nitroglycerin per spray after priming.

Additional Minor Change

1. The revision date was updated from NLPS-PI-1 Rev. 06/04 to NLPS-PI-2 Rev. 10/05.

The final printed labeling (FPL) must be identical to the patient package insert submitted October 28, 2005, except for the revision listed. These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as stated, in the product labeling may render the product misbranded and unapproved new drug.

1. In the **HOW SUPPLIED** section, the last sentence should be revised to read as follows:

   Each unit contains 4.9 g (NDC 59630- 300-65) or 12 g (NDC 59630-300-20) (Net Content) of nitroglycerin lingual spray which will deliver 60 or 200 metered sprays containing 400 mcgs of nitroglycerin per spray after priming.

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 supplement NDA 18-705, S-015** Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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:

Mr. John David
Regulatory Project Manager
(301) 796-1059

Sincerely,

Norman Stockbridge, M.D., Ph.D.
Acting Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Cc: Pohl Boskamp etc.

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

/s/

Norman Stockbridge

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