DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-943/S-013

Elan Drug Delivery, Inc.
Attention: Mr. Roger Wayne Wiley
1300 Gould Drive
Gainesville, GA 30504

Dear Mr. Wiley:

Please refer to your supplemental new drug application dated December 1, 2003 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Verelan PM (verapamil hydrochloride) 100, 200, and 300 mg extended-release capsules.

This supplemental new drug application provides for revisions to the **CLINICAL PHARMACOLOGY, PRECAUTIONS,** and **DOSAGE AND ADMINISTRATION** sections of the labeling. Information has been added that the Verelan PM capsule can be sprinkled over applesauce for ease of administration.

The proposed changes to the labeling are as follows:

1. Under **CLINICAL PHARMACOLOGY/Pharmacokinetics and metabolism** the following paragraph was added after the 6th paragraph:

   When the contents of Verelan PM capsule were administered by sprinkling onto one tablespoonful of applesauce, the rate and extent of verapamil absorption were found to be bioequivalent to the same dose when administered as an intact capsule. Similar results were observed with norverapamil.

2. Under **PRECAUTIONS**, the following sentence was added after the first sentence:

   Verelan PM CAPSULES ARE TO BE SWALLOWED WHOLE OR THE ENTIRE CONTENTS OF THE CAPSULE SPRINKLED ONTO APPLESAUCE (see DOSAGE AND ADMINISTRATION).

3. Under **PRECAUTIONS/General/Use in patients with impaired renal function,** the following sentence was added to the end of the paragraph:

   These patients should be carefully monitored for abnormal prolongation of the PR interval or other signs of overdosage (See **OVERDOSAGE**).

4. A new subsection entitled "**Information for Patients**" was added after the **PRECAUTIONS/General** section and reads as follows:

   Information for Patients
   When the sprinkle method of administration is prescribed, details of the proper technique should be explained to the patient. (See **DOSAGE and ADMINISTRATION**.)

5. Under **DOSAGE AND ADMINISTRATION**, a paragraph was added after the fourth paragraph and reads as follows:

   Sprinkling the Capsule Contents on Food
   Verelan PM capsules may also be administered by carefully opening the capsule and sprinkling the pellets onto one tablespoonful of applesauce. The applesauce should be swallowed immediately without chewing and followed with a glass of cool water to ensure complete swallowing of the pellets. The applesauce used should not be hot, and it should be soft enough to be swallowed without chewing. Any pellet/applesauce mixture should be used immediately and not stored for future use. Absorption of the pellets sprinkled onto other foods has not been tested. This method of administration may be beneficial for patients who have difficulty swallowing whole capsules or tablets. Subdividing the contents of a Verelan PM capsule is not recommended.

We have completed our review of this application and 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 revision listed below.

Under DOSAGE AND ADMINISTRATION/ Sprinkling the Capsule Contents on Food, the words (b)(4)------ should be deleted from the 6 th sentence. This subsection should now read as follows:

Sprinkling the Capsule Contents on Food
Verelan PM capsules may also be administered by carefully opening the capsule and sprinkling the pellets onto one tablespoonful of applesauce. The applesauce should be swallowed immediately without chewing and followed with a glass of cool water to ensure complete swallowing of the pellets. The applesauce used should not be hot, and it should be soft enough to be swallowed without chewing. Any pellet/applesauce mixture should be used immediately and not stored for future use. Absorption of the pellets sprinkled onto other foods has not been tested. This method of administration may be beneficial for patients who have difficulty swallowing whole capsules. Subdividing the contents of a Verelan PM capsule is not recommended.

Please submit the FPL electronically 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, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-943/S-013." Approval of this submission by FDA is not required before the labeling is used.

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:

Ms. Denise M. Hinton
Regulatory Health Project Manager
(301) 594-5333

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D.
Acting Director
Division of Cardio-Renal Drug Products
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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/

Norman Stockbridge

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