DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 13-217/S-044

Elan Pharmaceuticals, Inc.
Attention: Ms. Linda B. Fischer
Director, Regulatory Affairs
45 Horse Hill Road
Cedar Knolls, NJ 07927

Dear Ms. Fischer:

Please refer to your supplemental new drug application dated 16 October 2001, received 17 October 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Skelaxin (metaxalone) Tablets, 400mg.

This supplemental new drug application provides for inclusion of a Pharmacokinetics section in the label.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the following labeling:

Pharmacokinetics

In a single center, randomized, two-period crossover study with 42 healthy volunteers (31 males, 11 females), a single 400mg Skelaxin (metaxalone) tablet was administered under both fasted and fed conditions. Under fasted conditions, mean ± S.D. peak plasma metaxalone concentrations (C_{max}) of 983.4 ± 516.9 ng/mL were achieved within 3.3 ± 1.2 hours after dosing (T_{max}). Metaxalone concentrations declined with mean terminal half-life ($t_{1/2}$) of 9.0 ± 4.8 hours. The mean apparent oral clearance (CL/F) of metaxalone was 53.5 ± 27.1 L/hr. In the same study, the administration of a 400 mg Skelaxin tablet following a standardized high fat meal showed an increase in the mean C_{max} and the area under the curve (AUC_{0-t}) of metaxalone to 177.5% and 123.5%, respectively. The mean T_{max} was also increased to 4.3 ± 2.3 hr, whereas the mean $t_{1/2}$ was decreased to 2.4 ± 1.2 hr. Given the magnitude of plasma level changes following a high fat meal, Skelaxin tablets should be administered on an empty stomach.

The absolute bioavailability of Skelaxin tablets is not known. Metaxalone is metabolized by the liver and excreted in urine as unidentified metabolites.

The impact of age, gender, hepatic and renal disease on the pharmacokinetics of Skelaxin tablets has not been determined at this time.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). 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. 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 supplement NDA 13-217/S-044." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Jane A. Dean, RN, MSN, Regulatory Health Project Manager, at 301-827-2090.

Sincerely,

[See appended electronic signature page]

Lee S. Simon, M.D.
Division Director
Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products
Office of Drug Evaluation V
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/

Lee Simon
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