



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022195/S-002

Roxane Laboratories, Inc.
1809 Wilson Rd.
Columbus, OH 43228

Attention: Elizabeth Ernst
Director, Drug Regulatory Affairs and Medical Affairs

Dear Ms. Ernst:

Please refer to your supplemental new drug application dated August 25, 2009, received August 26, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Morphine Sulfate Oral Solution, 100 mg per 5 mL (20 mg/mL).

We acknowledge receipt of your submissions dated October 30, November 5 and 18, and December 1, 9, 17 and 18, 2009, and January 12, 2010.

This "Prior Approval" supplemental new drug application provides for the addition of the 100 mg per 5 mL (20 mg/mL) strength of Morphine Sulfate Oral Solution to your already-approved 20 mg/5 mL and 10 mg/5mL product line.

We have completed our review of this application, as amended, and it is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed upon labeling text which is identical to the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format submitted on December 17, 2009. We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your December 17, 2009, submission containing final printed carton and container labels.

PROPRIETARY NAME

If you intend to have a proprietary name for this product, we recommend that you submit a request for a proposed proprietary name review. (See the draft Guidance for Industry, *Complete Submission for the Evaluation of Proprietary Names*, at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075068.pdf> and “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012”.)

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable. This is because the number of pediatric patients requiring this medication is small.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)).

Since Morphine Sulfate Oral Solution was approved on March 27, 2008, we have become aware of post-marketing reports of prescriptions for a 20-mg dose being administered as a 20-mL dose. A 20-mL dose would result in a 40-mg, 80-mg or 400-mg dose depending on which concentration was available. Such errors have resulted in life-threatening overdoses. Given that supplement S-002 proposes the addition of a 20-mg/mL strength of Morphine Sulfate Oral Solution, the risk of medication errors will likely increase when the 20-mg/mL formulation is approved. We consider this information to be “new safety information” as defined in section 505-1(b) of FDCA.

Your proposed REMS, submitted on January 12, 2010, and appended to this letter, is approved. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS.

The REMS assessment plan should include but is not limited to the following:

- a. An evaluation of patients' understanding of the serious risks of Morphine Sulfate Oral Solution
- b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
- c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

Assessments of an approved REMS must also include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 022195 REMS ASSESSMENT

**NEW SUPPLEMENT FOR NDA 022195
PROPOSED REMS MODIFICATION
REMS ASSESSMENT**

**NEW SUPPLEMENT FOR (NEW INDICATION FOR USE)
FOR NDA 022195
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

PROMOTIONAL MATERIALS

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the following address or by facsimile at 301-847-8444:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

In addition, as required under 21 CFR 314.81(b)(3)(i), you must submit your updated final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA-2253, directly to the above address. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

EXPIRATION DATING PERIOD

An expiration dating period of 18 months is granted to the Morphine Sulfate Oral Solution 20 mg/mL in HDPE bottles, stored at 20-25°C, excursion permitted to 15-30°C (59°-86°F).

LETTERS TO HEALTH CARE PROFESSIONALS

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

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

REPORTING REQUIREMENTS

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 Lisa Basham, Regulatory Project Manager, at (301) 796-1175.

Sincerely,

{See appended electronic signature page}

Sharon Hertz, MD
Deputy Division Director
Division of Anesthesia, Analgesia and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:

Content of Labeling
Carton and Container Labeling
REMS

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22195

SUPPL-2

ROXANE
LABORATORIES
INC

MORPHINE SULPHATE ORAL
SOLUTION

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

/s/

SHARON H HERTZ

01/25/2010