CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

202515Orig1s000

Trade Name:	Morphine sulfate injection USP, 2, 4, 8, 10, and 15 mg/mL in Carpuject and iSecure syringes
Generic Name:	Morphine sulfate
Sponsor:	Hospira, Inc.
Approval Date:	November 14, 2011
Indications:	Use of morphine sulfate injection, USP, for the management of pain not responsive to non-narcotic analgesics.

CENTER FOR DRUG EVALUATION AND RESEARCH

202515Orig1s000

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	**X**
Other Action Letters	
Labeling	**X**
REMS	
Summary Review	**X**
Officer/Employee List	**X**
Office Director Memo	
Cross Discipline Team Leader Review	
Medical Review(s)	**X**
Chemistry Review(s)	**X**
Environmental Assessment	
Pharmacology Review(s)	**X**
Statistical Review(s)	
Microbiology Review(s)	**X**
Clinical Pharmacology/Biopharmaceutics Review(s)	**X**
Other Reviews	**X**
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	
Administrative/Correspondence Document(s)	**X**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202515Orig1s000

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202515

NDA APPROVAL

Hospira, Inc.
275 North Field Drive
Dept. 0389, Bldg. H2-2
Lake Forest, IL 60045-5046

Attention: Melissa A. Nguyen
Product Manager, Regulatory Affairs

Dear Ms. Nguyen:

Please refer to your New Drug Application (NDA) dated January 14, 2011, received January 14, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for morphine sulfate injection USP, 2, 4, 8, 10, and 15 mg/mL in Carpuject and iSecure syringes.

We acknowledge receipt of your amendments dated January 25, February 11, March 7 and 22, April 15, May 17, June 28, July 12, 14, and 26, August 22, September 14, October 14, 17, 19, and 27, and November 7, 9, and 11, 2011.

This new drug application provides for the use of morphine sulfate injection, USP, for the management of pain not responsive to non-narcotic analgesics.

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 enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 202515**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

PROPRIETARY NAME

If you intend to have a proprietary name for this product, the name and its use in the labels must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit a request for a proposed proprietary name review. (See the guidance for industry titled, "Contents of a 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.

Because none of these criteria apply to your application, you are exempt from this requirement.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify unexpected serious risk of genotoxicity or histopathological changes associated with exposure to the drug substance impurities, [redacted] (b) (4) at the proposed levels.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

1836-1 Conduct an in vitro genetic toxicology study to detect point mutations with the isolated drug product impurity [redacted] (b) (4), tested up to the limit dose for the assay.

The timetable you submitted on October 27, 2011, states that you will conduct this study according to the following schedule:

Study Completion: April 2012
Final Report Submission: July 2012

1836-2 Conduct an in vitro genetic toxicology study to detect point mutations with the isolated drug product impurity [redacted] (b) (4), tested up to the limit dose for the assay.

The timetable you submitted on October 27, 2011, states that you will conduct this study according to the following schedule:

Study Completion: April 2012
Final Report Submission: July 2012

1836-3 Conduct an in vitro genetic toxicology study to detect chromosome aberrations with the isolated drug product impurity [redacted] (b) (4) tested up to the limit dose for the assay.

The timetable you submitted on October 27, 2011, states that you will conduct this study according to the following schedule:

Study Completion: April 2012
Final Report Submission: July 2012

1836-4 Conduct an in vitro genetic toxicology study to detect chromosome aberrations with the isolated drug product impurity [redacted] (b) (4), tested up to the limit dose for the assay.

The timetable you submitted on October 27, 2011, states that you will conduct this study according to the following schedule:

Study Completion:	April 2012
Final Report Submission:	July 2012

1836-5 Conduct a 3-month repeat-dose toxicology study in a single species with the following drug product impurities: [redacted] (b) (4).

The timetable you submitted on October 27, 2011, states that you will conduct this study according to the following schedule:

Study Completion:	June 2012
Final Report Submission:	October 2012

Submit all final reports to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **"Required Postmarketing Protocol Under 505(o)", "Required Postmarketing Final Report Under 505(o)", "Required Postmarketing Correspondence Under 505(o)"**.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. 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

The proposed expiry of twenty-four (24) months for Carpuject™ and iSecure™ syringes when stored at controlled room temperature (20 to 25°C; 68 to 77°F) is granted.

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 Kimberly A. Compton, R.Ph., Senior Regulatory Project Manager at (301) 796-1191.

Sincerely,

{See appended electronic signature page}

Sharon H. Hertz, M.D.
Deputy Director
Division of Anesthesia, Analgesia, and Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Carton and Container Labeling

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
11/14/2011