

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

022396Orig1s000

Trade Name: Dyloject Injection

Generic Name: Diclofenac Sodium

Sponsor: **JAVELIN PHARMACEUTICALS, INC**

Approval Date: December 23, 2014

Indications: Dyloject is an Non-steroidal anti-inflammatory drug (NSAID) indicated in adults for the management of mild to moderate pain and management of moderate to severe pain alone or in combination with opioid analgesics.

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APPROVAL LETTER



NDA 022396

NDA APPROVAL

Javelin Pharmaceuticals, Inc.
c/o Hospira, Inc.
275 North Field Dr.
Dept. 0392, Bldg. H2-2
Lake Forest, IL 60045

Attention: Steven Townsend
Associate Director, Global Regulatory Affairs

Dear Mr. Townsend:

Please refer to your New Drug Application (NDA) dated December 2, 2009, received December 3, 2009, submitted pursuant to Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Dyloject (diclofenac sodium) Injection 37.5 mg/mL.

We acknowledge receipt of your amendments dated December 22, 2009, January 14, March 8, 18, and 23, April 8, 23, 27, and 28, May 6, 25, and 26, June 1, 2, 10 (2), 16, and 17 (2), July 8 (2), 12, 19, and 28, August 11, 19, and 25, September 9, 20, 21(2), 23, 27, 28 (2), and 29, 2010, September 22 and November 8, 2011, June 28, July 30, August 26, October 31, November 20, December 17, 2013, and October 31, November 21, and December 09, 2014.

The October 31, 2014, submission constituted a complete response to our December 23, 2013, action letter.

Reference is also made to your email dated December 22, 2014, which included the final agreed-upon labeling.

This new drug application provides for the use of Dyloject (diclofenac sodium) Injection 37.5 mg/mL for the management of mild to moderate pain and management of moderate to severe pain alone or in combination with opioid 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 *SPL Standard for Content of Labeling Technical Qs and As*, available 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 immediate container labels that are identical to the enclosed carton and immediate container labels and carton and immediate container labels submitted on December 17, 2013, 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 *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 022396.**” 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.

MARKET PACKAGE

Please submit one market package of the drug product when it is available to the following address:

Swati Patwardhan
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 3170
10903 New Hampshire Avenue
Silver Spring, Maryland
*Use zip code **20903** if shipping via United States Postal Service (USPS).*
*Use zip code **20993** if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

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 ages birth to less than 1 year because there is evidence strongly suggesting that the drug product would be unsafe in this pediatric age group.

We are deferring submission of your pediatric studies for ages 2 to less than 17 years because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required under Section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and Section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

2839-1 An open-label pharmacokinetic and safety study or studies of an age-appropriate formulation of Dyloject (diclofenac sodium) Injection in pediatric patients 2 to less than 17 years of age with acute pain.

Final Protocol Submission:	06/17
Study Completion:	03/19
Final Report Submission:	09/19

2839-2 A pharmacokinetic, safety, and efficacy study or studies of an age-appropriate formulation of Dyloject (diclofenac sodium) Injection in pediatric patients 1 to less than 2 years of age with acute pain. Conduct the study or studies after the juvenile animal toxicology study of Dyloject is completed (PMR 2839-3).

Final Protocol Submission:	04/19
Study Completion:	05/20
Final Report Submission:	11/20

2839-3 A juvenile animal study to evaluate the general toxicology of the Dyloject (diclofenac sodium) Injection pediatric formulation to support the safe use of the pediatric formulation prior to initiation of the clinical study in pediatric patients 1 through less than 2 years of age (PMR 2839-2).

The timetable you submitted on December 09, 2014, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	05/17
Study Completion:	03/18
Final Report Submission:	07/18

Submit the protocols to your IND 65048, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

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
Office of Prescription Drug Promotion
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. Form FDA 2253 is available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>. Information and Instructions for completing the form can be found at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

EXPIRY DATING PERIOD

A 18-month expiry dating period is granted for Dyloject (diclofenac sodium) Injection 37.5 mg/mL, when stored at 20° to 25°C (68° to 77°F) [see USP].

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 Swati Patwardhan, Regulatory Project Manager, at (301) 796-4085.

Sincerely,

{See appended electronic signature page}

Rigoberto A. Roca, MD
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/

RIGOBERTO A ROCA
12/23/2014