CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-745

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-745

NDA APPROVAL

Labopharm Canada, Inc.
c/o CanReg Inc.
450 North Lakeshore Dr.
Mundelein, IL 60060

Attention: Becky Prokipcak, Ph.D., RAC
Sr. Director, Regulatory Affairs, CanReg Inc.
U.S. Agent for Labopharm Canada, Inc.

Dear Dr. Prokipcak:

Please refer to your new drug application (NDA) dated November 25, 2005, received November 28, 2008, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Ryzolt™ (tramadol hydrochloride extended-release tablets) 100 mg, 200 mg, and 300 mg.

We acknowledge receipt of your submissions dated March 1, 20 and 28, April 6 and 7, May 2, 24, 25, and 31, June 12, 16, 20, 23, and 27, July 25, August 8, 18, 23, and 29, and December 18, 2006, and February 8 and 28, March 1, and April 30, 2007, and July 2, and December 29, 2008.

The July 2, 2008, submission constituted a complete response to our May 30, 2007, action letter.

This new drug application provides for the use of Ryzolt™ (tramadol hydrochloride extended-release tablets) for the management of moderate to moderately severe chronic pain in adults who require around-the-clock treatment of their pain for an extended period of time.

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.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling text. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. **For administrative purposes, please designate this submission, "SPL for approved NDA 21-745."**

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your December 29, 2008, submission containing final printed carton and container labels.

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 0 to < 2 years because necessary studies are impossible or highly impracticable. This is because there are too few patients in this age range who require treatment for chronic pain using an oral modified-release analgesic to be able to conduct clinical trials.

We are deferring submission of your pediatric study for ages ≥ 2 to 17 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

1. **To study the pharmacokinetics, efficacy and safety of Ryzolt™ for the the management of** moderate to moderately severe chronic pain in pediatric patients ages ≥ 2 to 17 years.

   Final Report Submission: January 2014

Submit final study reports to this NDA. For administrative purposes, all submissions related to this required pediatric postmarketing **study must be clearly designated "Required Pediatric Assessment".**

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(s) 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 www.fda.gov/cder/ddmac.

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
Suite 12B05
5600 Fishers Lane
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 Kathleen Davies, Regulatory Project Manager, at (301) 796-2205.

Sincerely,

{See appended electronic signature page}

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

Enclosure: Package Insert

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

/s/

Sharon Hertz
12/30/2008 12:56:44 PM