CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 091607

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 091607

Caraco Pharmaceutical Laboratories, Ltd.
U.S. Agent for: Sun Pharma Global FZE
Attention: Robert Kurkiewicz
Senior V.P., Regulatory Affairs
1150 Elijah McCoy Drive
Detroit, MI 48202

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated June 13, 2009, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Tramadol Hydrochloride Extended-release Tablets, 100 mg, 200 mg, and 300 mg (Once Daily).

Reference is also made to the tentative approval letter issued by this office on November 30, 2011, and to your amendment dated December 1, 2011.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Tramadol Hydrochloride Extended-release Tablets, 100 mg, 200 mg, and 300 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Ryzolt Tablets 100 mg, 200 mg and 300 mg, respectively, of Purdue Pharma Products L.P. (Purdue).

Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA. The “interim” dissolution specifications are as follows:

> Dissolution testing should be conducted in 900 mL of 0.1N HCl, at 37^{o}C +/- 0.5^{o}C, using USP Apparatus I (Basket), at 75 rpm. The test product should meet the following “interim” specifications:

Time (Hours)	Percent Dissolved
2	(b) (4)
4	
8	
10	
16	

The “interim” dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a “Special Supplement – Changes Being Effected” if there are no revisions to be made to the “interim” specifications, or if the final specifications are tighter than the “interim” specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

The RLD upon which you have based your ANDA, Purdue’s Ryzolt Extended-release Tablets, is subject to periods of patent protection. The following patents and their expiration dates are currently listed in the agency’s publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the “Orange Book”) for this drug product:

U.S. Patent Number	Expiration Date
5,591,452 (the ‘452 patent)	May 10, 2014
6,254,887 (the ‘887 patent)	May 10, 2014
6,607,748 (the ‘748 patent)	June 29, 2020
7,988,998 (the ‘998 patent)	October 27, 2023

Your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that each of these patents is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Tramadol Hydrochloride Extended-release Tablets, 100 mg, 200 mg, and 300 mg, under this ANDA. You have notified the agency that Sun Pharma Global FZE (Sun) complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation for infringement of the ‘887 patent was initiated against Sun within the statutory 45-day period in the United States District Court for the District of Delaware[Civil Action No. 09-833-KAJ].[1] You have also notified

[1] It is noted that the ‘998 patent was listed after submission of your ANDA and your paragraph IV certification was submitted in an amendment to your ANDA. Litigation, if any, with respect to the ‘998 patent will therefore not delay approval of your ANDA.

the agency that the court decided that the '887 patent is invalid.[2]

With respect to 180-day generic drug exclusivity, we note that Sun was the first ANDA applicant to submit a substantially complete ANDA for Purdue's Ryzolt Extended-release Tablets (Tramadol Hydrochloride Extended-release Tablets, 100 mg, 200 mg, and 300 mg,) with a paragraph IV certification. Therefore, with this approval, Sun is eligible for 180 days of generic drug exclusivity for Tramadol Hydrochloride Extended-release Tablets, 100 mg, 200 mg, and 300 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act, will begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). Within 10 days of first commercial marketing, please submit correspondence to this ANDA informing the agency of the date you begin commercial marketing of Tramadol Hydrochloride Extended-release Tablets, 100 mg, 200 mg, and 300 mg. Please also be aware that, under section 505(j)(5)(D), the 180-day exclusivity shall be forfeited by Sun if a forfeiture event, as described in section 505(j)(5)(D), occurs with respect to Sun.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

[2] You have informed the agency that Sun was also sued for infringement of U.S. Patent No. 7,074,430, which is not listed in the Orange Book. Although litigation with respect to an unlisted patent will not delay approval of an ANDA, it is noted that the court found this patent, as well as the '887 patent, to be invalid.

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Office of Prescription Drug Promotion with a completed Form FDA 2253 at the time of their initial use.

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). 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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/U_CM072392.pdf. The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
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/

ROBERT L WEST

12/30/2011

Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.