DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 022304/S-007, S-008, S-009, S-011, S-012

SUPPLEMENTS APPROVAL
RELEASE REMS REQUIREMENT

Janssen Research & Development, L.L.C.
on behalf of Janssen Pharmaceuticals, Inc.
920 Route 202 South
P.O. Box 300
Raritan, NJ 08869

Attention: Tania Hillmer, MS, RAC
Associate Director, Regulatory Affairs

Dear Ms. Hillmer:

Please refer to your following Supplemental New Drug Applications (sNDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Nucynta (tapentadol) immediate-release (IR) oral tablets, 50 mg, 75 mg, and 100 mg.

Supplement Number	Submission Date	Receipt Date
S-007	December 16, 2010	December 16, 2010
S-008	December 21, 2010	December 21, 2010
S-009	March 16, 2011	March 16, 2011
S-011	August 25, 2011	August 26, 2011
S-012	November 29, 2011	November 29, 2011

We acknowledge receipt of your amendments to Supplement-8 dated July 12, 2012, and May 10, 2013, and your risk evaluation and mitigation strategy (REMS) assessment dated November 29, 2011.

S-007, submitted as a "Changes Being Effected" supplemental new drug application, provides for the addition of "Angioedema" to section **6 ADVERSE REACTIONS**, subsection **6.3 Post-marketing Experience** of the Package Insert**.**

S-008, submitted as a "Prior Approval" supplemental new drug application, proposes revisions to the Package Insert and Medication Guide with the addition of "hypersensitivity" as a contraindication, proposes additional revisions to the Medication Guide to describe "angioedema" as a possible side effect, and, as amended on July 12, 2012, following discussions with FDA, proposes withdrawal of the Medication Guide as part of the Nucynta IR tablet labeling.

S-009, submitted as a "Changes Being Effected" supplemental new drug application, provides for the addition of "Diarrhea" to section **6 ADVERSE REACTIONS**, subsection **6.3 Post-marketing Experience** of the Package Insert**.**

S-011, submitted as a "Changes Being Effected" supplemental new drug application, provides for the addition of "Palpitations" to section **6 ADVERSE REACTIONS**, subsection **6.3 Post-marketing Experience** of the Package Insert**.**

S-012, submitted as a "Prior Approval" supplemental new drug application, proposes to eliminate the requirement for the approved REMS for Nucynta IR tablets.

We have completed our review of these supplemental applications, as amended. They are 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 physicians, with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Nucynta IR tablets was originally approved on November 20, 2008. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS.

You propose that FDA no longer require a REMS for Nucynta IR tablets.

The requirement of a REMS for Nucynta IR tablets was, at the time of its approval, consistent with the Agency's policies concerning drug products with Medication Guides to address serious and significant public health concerns under the standard in 21 CFR 208.1. However, during the four years of marketing history of Nucynta IR tablets, the concerns about this product having distinctive properties indicating a high potential for abuse did not manifest as serious adverse events of abuse/misuse any different or worse than other immediate-release oral opioids which do not have Medication Guides. We agree with your proposal that the Medication Guide be eliminated as part of the approved labeling for Nucynta IR tablets. We agree also that the REMS for Nucynta IR tablets can now be eliminated.

Therefore, a REMS for Nucynta IR tablets is no longer required.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. 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.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in 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 address above or by fax to 301-847-8444.

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 Dominic Chiapperino, Ph.D., Senior Regulatory Health Project Manager, at (301) 796-1183.

Sincerely,

{See appended electronic signature page}

Bob A. Rappaport, M.D.
Director
Division of Anesthesia, Analgesia, and Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

BOB A RAPPAPORT
07/11/2013