CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

204031Orig1s000

Trade Name:	Xartemis XR Extended-Release Tablets, 7.5 mg/325 mg.
Generic Name:	oxycodone hydrochloride and acetaminophen
Sponsor:	Mallinckrodt Inc.
Approval Date:	March 11, 2014
Indications:	for the management of acute pain severe enough to require opioid treatment and for which alternative treatment options are inadequate.

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204031Orig1s000

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APPLICATION NUMBER:

204031Orig1s000

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 204031

NDA APPROVAL

Mallinckrodt Inc.
675 McDonnell Blvd.
Hazelwood, MO 63042

Attention: Kevin D. Healy
Associate Director Regulatory Affairs

Dear Mr. Healy:

Please refer to your New Drug Application (NDA) dated May 24, 2013, received May 28, 2013, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Xartemis XR (oxycodone hydrochloride and acetaminophen) Extended-Release Tablets, 7.5 mg/325 mg.

We acknowledge receipt of your amendments dated July 18, August 12 and 23, September 27, October 4, 11, 17 (2), 22, 24, and 25, and November 8, 11, 18, and 22, 2013, and January 10 and 22, and February 24, 2014.

This new drug application provides for the use of Xartemis XR (oxycodone hydrochloride and acetaminophen) Extended-Release Tablets for the management of acute pain severe enough to require opioid treatment and for which alternative treatment options are inadequate.

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.

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 and Medication Guide). 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 identical to the carton and immediate container labels submitted on November 22, 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 204031**." 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.

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 deferring submission of your pediatric studies until April 1, 2020, 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.

2131-1 Conduct an open-label pharmacokinetics and safety study of Xartemis XR in pediatric patients ages 12 to less than 17 years with acute pain severe enough to require opioid treatment and for which alternative treatment options are inadequate.

Final Protocol Submission:	April 30, 2014
Study/Trial Completion:	November 1, 2015
Final Report Submission:	March 31, 2016

2131-2 Conduct an open-label pharmacokinetics and safety study of an age-appropriate formulation (oxycodone hydrochloride/acetaminophen) in pediatric patients ages 2 to less than12 years with acute pain severe enough to require opioid treatment and for which alternative treatment options are inadequate.

Final Protocol Submission: July 1, 2016
Study/Trial Completion: January 1, 2018
Final Report Submission: June 1, 2018

2131-3 Conduct a pharmacokinetics, safety, and efficacy study of an age-appropriate formulation (oxycodone hydrochloride/acetaminophen) in pediatric patients ages 0 (birth) to less than 2 years with acute pain severe enough to require opioid treatment and for which alternative treatment options are inadequate.

Final Protocol Submission: September 1, 2018
Study/Trial Completion: March 1, 2020
Final Report Submission: July 1, 2020

Submit the protocols to your IND 104702, 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.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

We acknowledge receipt of your submission dated May 24, 2013, and amended October 25, 2013, of a proposed risk evaluation and mitigation strategy (REMS). We have determined that, at this time, a REMS is not necessary for Xartemis XR to ensure that its benefits outweigh its risks. We will notify you if we become aware of new safety information and make a determination that a REMS is necessary.

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. For instruction on completing the Form FDA 2253, see 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.

EXPIRY DATING PERIOD

A 24-month expiry dating period is granted for Xartemis XR in 100-count, 150 cc HDPE bottles when stored at 25°C (77°F) with excursions permitted from 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

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, PhD, Senior Regulatory Health Project Manager, at (301) 796-1183.

Sincerely,

{See appended electronic signature page}

Sharon Hertz, MD
Deputy Director
Division of Anesthesia, Analgesia, and
Addiction products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:
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
03/11/2014