



NDA 210450

NDA APPROVAL

AbbVie Inc.
Attention: Glen W. Spears, Ph.D.
Director, Regulatory Affairs
1 N. Waukegan Road
Dept. PA72/Bldg. AP30-4
North Chicago, Illinois 60064

Dear Dr. Spears:

Please refer to your New Drug Application (NDA) dated and received August 23, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Orilissa (elagolix sodium) oral tablets 150 mg and 200 mg.

We acknowledge receipt of your major amendment dated March 19, 2018, which extended the goal date by three months.

This new drug application provides for the use of Orilissa (elagolix sodium) tablets for the management of moderate to severe pain associated with endometriosis.

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 prescribing information, 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

We acknowledge your July 12, 2018, submission containing final printed carton and container labels.

ADVISORY COMMITTEE

This application was not referred to an FDA advisory committee because the application did not raise significant public health questions on the role of the drug in the diagnosis, mitigation, treatment, or prevention of a disease.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving this requirement for your application because this product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients and is not likely to be used in a substantial number of pediatric patients.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify an unexpected serious risk of adverse pregnancy, maternal, and fetal/neonatal outcomes associated with exposure to Orilissa, and safety outcomes associated with co-administration of a combined oral contraceptive (containing ethinyl estradiol and levonorgestrel) with Orilissa.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies and trial:

- 3390-1 A prospective pregnancy registry to evaluate the effects of Orilissa on pregnancy and maternal and fetal/neonatal outcomes.

The timetable you submitted on July 18, and July 23, 2018, states that you will conduct this study according to the following schedule:

Final Protocol Submission: January 2019
Interim Reports: January 2021, January 2023, January 2025,
January 2027
Study Completion: January 2029
Final Report Submission: January 2030

- 3390-2 A pharmacoepidemiology surveillance study to evaluate the effects of Orilissa on pregnancy-related outcomes.

The timetable you submitted on July 18, and July 23, 2018, states that you will conduct this study according to the following schedule:

Final Protocol Submission: January 2019
Interim Report: January 2023
Study Completion: January 2024
Final Report Submission: January 2025

- 3390-3 A drug-drug interaction trial to assess the pharmacokinetics, safety, and tolerability of the co-administration of a combined oral contraceptive (containing ethinyl estradiol and levonorgestrel) with Orilissa 200 mg twice daily.

The timetable you submitted on July 18, 2018, states that you will conduct this trial according to the following schedule:

Final Protocol Submission: October 2018
Study/Trial Completion: October 2019
Final Report Submission: April 2020

Submit clinical protocols to your IND 64802 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final reports to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **Required Postmarketing Protocol Under 505(o), Required Postmarketing Final Report Under 505(o), Required Postmarketing Correspondence Under 505(o).**

Submission of the protocols for required postmarketing observational studies to your IND is for purposes of administrative tracking only. These studies do not constitute clinical investigations pursuant to 21 CFR 312.3(b) and therefore are not subject to the IND requirements under

21 CFR part 312 or FDA's regulations under 21 CFR parts 50 (Protection of Human Subjects) and 56 (Institutional Review Boards).

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

- 3390-4 A randomized, controlled clinical trial to assess the effects of a combined hormonal contraceptive on the efficacy of Orilissa in women with moderate to severe pain associated with endometriosis. This trial will also assess the effects of Orilissa on the efficacy of the combined hormonal contraceptive, and safety with concomitant use of Orilissa and the combined hormonal contraceptive.

Per communication on July 19, 2018, the timetable you submitted states that you will conduct this study according to the following schedule:

Final Protocol Submission:	February 2019
Study/Trial Completion:	August 2022
Final Report Submission:	February 2023

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 prescribing information, Medication Guide, and patient PI (as applicable) to:

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

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the prescribing information, 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>.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

As agreed to in your submission dated June 29, 2018, you will conduct enhanced pharmacovigilance of Orilissa for hepatic adverse events, including liver injury. For a period of 3 years, submit expedited 15-day Alert reports (as described under 21 CFR 314.80(c)(1)) and review all reports of hepatic adverse events, including liver injury. Provide detailed analyses of hepatic adverse events, including liver injury reported from clinical study and post-marketing reports in your periodic safety reports. These analyses should discuss cumulative data relative to the date of approval of Orilissa. Also, provide medical literature reviews for case reports/case series of hepatic adverse events, including liver injury reported with Orilissa in the periodic safety reports. The enhanced pharmacovigilance program will be reassessed 3 years after Orilissa approval.

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment

instructions and program description details
at <http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm>.

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Maria Wasilik, Regulatory Project Manager, at (301) 796-0567.

Sincerely,

{See appended electronic signature page}

Victor Crentsil, M.D., M.H.S.
Acting Deputy Director
Office of Drug Evaluation III
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. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

VICTOR CRENTSIL
07/23/2018