

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

206500Orig1s000

Trade Name: Varubi Tablets 90 mg

Generic Name: rolapitant

Sponsor: TESARO, Inc.

Approval Date: September 1, 2015

Indication: For prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

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APPLICATION NUMBER:

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APPROVAL LETTER



NDA 206500

NDA APPROVAL

TESARO, Inc.
Attention: Gabriela Rossi
Director, Regulatory Affairs
1000 Winter Street, Suite 3300
Waltham, MA 02451

Dear Ms. Rossi:

Please refer to your New Drug Application (NDA) dated and received September 5, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Varubi (rolapitant) Tablets 90 mg.

We acknowledge receipt of your amendments dated August 31, 2015; August 24, 2015; August 21, 2015; August 20, 2015; August 18, 2015; August 12, 2015; August 5, 2015; July 29, 2015; July 17, 2015; July 13, 2015; June 19, 2015; June 12, 2015; June 1, 2015; May 20, 2015; May 14, 2015; April 22, 2015; April 10, 2015; April 8, 2015; April 2, 2015; March 31, 2015; March 27, 2015; March 26, 2015; March 13, 2015; February 27, 2015; February 20, 2015; February 6, 2015; January 23, 2015; January 14, 2015; January 9, 2015; December 22, 2014; December 9, 2014; December 5, 2014; October 17, 2014; and October 7, 2014.

This new drug application provides for the use of Varubi (rolapitant) tablets for prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

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 agreed-upon labeling text and with the minor editorial revisions indicated in the enclosed labeling.

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, text for the

patient package insert). 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 carton labels submitted on August 31, 2015, and immediate container labels submitted on June 19, 2015, 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 206500.**” 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.

ADVISORY COMMITTEE

Your application for Varubi was not referred to an FDA advisory committee because it is not the first in its class and the application did not raise significant public health questions on the role of Varubi in the diagnosis, cure, mitigation, treatment, or prevention of a disease. Outside expertise was not necessary; and there were no controversial issues that would benefit from advisory committee discussion.

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 August 30, 2026, 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 Federal Food, Drug, and Cosmetic Act 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)(C) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

2879-1 A GLP toxicology study in juvenile rats

Final Report Submission: 1/30/2017

2879-2 A dose-ranging study assessing the pharmacokinetics, safety, tolerability, and effectiveness of Varubi (rolapitant) in pediatric patients ages 0-17 years old

Final Protocol Submission: 2/28/2017

Study Completion: 7/31/2020

Final Report Submission: 11/30/2020

2879-3 A study to evaluate the efficacy and safety of a single oral dose of Varubi (rolapitant) in pediatric patients ages 0-17 years old

Final Protocol Submission: 11/30/2020

Study Completion: 04/30/2026

Final Report Submission: 08/30/2026

Submit the protocols to your IND 72754, 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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

2879-4 In vivo drug interaction study with a sensitive substrate of CYP2D6 to study the duration of CYP2D6 inhibition beyond 7 days after a single dose administration of Varubi (rolapitant)

The timetable you submitted on August 13, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 12/31/2015
Study Completion: 04/30/2016
Final Report Submission: 06/30/2016

- 2879-5 In vitro studies to evaluate the inhibitory potential of Varubi (rolapitant) on renal transporters, i.e., organic cation transporter 2 (OCT2), multidrug and toxin extrusion (MATE) transporters, organic anion transporter 1 (OAT1), and organic anion transporter 3 (OAT3)

The timetable you submitted on August 13, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 12/31/2015
Study Completion: 04/30/2016
Final Report Submission: 06/30/2016

- 2879-6 In vitro study to evaluate the inhibitory potential of Varubi (rolapitant) on OATP1B1 and OATP1B3. The in vitro study results will determine the need for a subsequent clinical assessment of a drug interaction between Varubi (rolapitant) and other concomitant medications

The timetable you submitted on August 13, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 02/28/2016
Study Completion: 06/30/2016
Final Report Submission: 08/31/2016

Submit clinical protocols to your IND 72754 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **“Postmarketing Commitment Protocol,” “Postmarketing Commitment Final Report,” or “Postmarketing Commitment Correspondence.”**

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, 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 package insert, 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).

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.

PDUFA V APPLICANT INTERVIEW

FDA has contracted with Eastern Research Group, Inc. (ERG) to conduct an independent interim and final assessment of the Program for Enhanced Review Transparency and Communication for NME NDAs and Original BLAs under PDUFA V ('the Program'). The PDUFA V Commitment Letter states that these assessments will include interviews with applicants following FDA action on applications reviewed in the Program. For this purpose, first-cycle actions include approvals, complete responses, and withdrawals after filing. The purpose of the interview is to better understand applicant experiences with the Program and its ability to improve transparency and communication during FDA review.

ERG will contact you to schedule a PDUFA V applicant interview and provide specifics about the interview process. Your responses during the interview will be confidential with respect to the FDA review team. ERG has signed a non-disclosure agreement and will not disclose any identifying information to anyone outside their project team. They will report only anonymized results and findings in the interim and final assessments. Members of the FDA review team will be interviewed by ERG separately. While your participation in the interview is voluntary, your feedback will be helpful to these assessments.

If you have any questions, call Mary Chung, Regulatory Project Manager, at (301) 796-0260.

Sincerely,

{See appended electronic signature page}

Amy G. Egan, M.D., M.P.H.
Deputy Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure(s):

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/

AMY G EGAN
09/01/2015