

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

022524Orig1s000

Trade Name: ZUPLENZ oral soluble film, 4 mg and 8 mg.

Generic Name: ondansetron

Sponsor: Par Pharmaceutical, Inc.

Approval Date: July 2, 2011

Indications: This new drug application provides for the use of ZUPLENZ (ondansetron) oral soluble film for:

- Prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy, including cisplatin ≥ 50 mg/m²
- Prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy
- Prevention of nausea and vomiting associated with radiotherapy in patients receiving either total body irradiation, single high-dose fraction to abdomen, or daily fractions to the abdomen
- Prevention of postoperative nausea and/or vomiting

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APPROVAL LETTER



NDA 022524

NDA APPROVAL

Par Pharmaceutical, Inc.
Attention: Casilda Barnes, Pharm.D.
Director, Regulatory Affairs
300 Tice Boulevard
Woodcliff Lake, NJ 07677

Dear Dr. Barnes:

Please refer to your New Drug Application (NDA) dated April 7, 2009, received April 7, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for ZUPLENZ (ondansetron) oral soluble film, 4 mg and 8 mg.

We acknowledge receipt of your amendments dated May 1, 2009; August 10, 2009; September 22, 2009; October 19, 2009; November 4, 2009; January 11, 2010; May 4, 2010; June 22, 2010; and July 1, 2010.

The May 4, 2010, submission constituted a complete response to our February 5, 2010, action letter.

This new drug application provides for the use of ZUPLENZ (ondansetron) oral soluble film for:

- Prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy, including cisplatin ≥ 50 mg/m²
- Prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy
- Prevention of nausea and vomiting associated with radiotherapy in patients receiving either total body irradiation, single high-dose fraction to abdomen, or daily fractions to the abdomen
- Prevention of postoperative nausea and/or vomiting

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.

We acknowledge your request to waive the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. As previously discussed with you, we are denying your request.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via 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 to the enclosed labeling (text for the package insert and text for the patient package insert). 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/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 container labels that are identical to the enclosed carton and immediate container labels 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 titled “Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)”. 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 022524.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product 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 waiving the pediatric study requirement for the indication prevention of nausea and vomiting associated with radiotherapy in patients receiving either total body irradiation, single high-dose fraction to abdomen, or daily fractions to the abdomen because necessary studies are impossible or highly impracticable. There are too few children with radiotherapy-induced nausea and vomiting to study.

We are waiving the pediatric study requirement for children less than 4 years of age for the following indications:

- prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy, including cisplatin ≥ 50 mg/m²; and
- prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy

because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group and is not likely to be used in a substantial number of pediatric patients in this group. There are age-appropriate formulations of alternative antiemetic products for these indications.

We are deferring submission of your pediatric studies for the following indications and age groups:

- prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy, including cisplatin ≥ 50 mg/m² in children ages 4 to less than 17 years; and
- prevention of postoperative nausea and/or vomiting in children ages 0 to less than 17 years

because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by 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)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1664-1 Deferred pediatric study under PREA for the prevention of nausea and vomiting in pediatric cancer patients ages 4 to <17 years receiving highly emetogenic chemotherapy (HEC). A PK and safety study to characterize the pharmacokinetics of Zuplenz (ondansetron) oral soluble film in pediatric patients ages 4 to <17 years receiving HEC.

Final Protocol Submission: June 2011
Study/Trial Completion: June 2012
Final Report Submission: December 2012

1664-2 Deferred pediatric study under PREA for the prevention of nausea and vomiting in pediatric cancer patients ages 4 to <17 years receiving HEC. An adequately powered, well-controlled, and randomized dose-response study to evaluate the safety and efficacy of Zuplenz (ondansetron) oral soluble film compared to standard therapy in pediatric patients ages 4 to <17 years receiving HEC.

Final Protocol Submission: December 2013
Study/Trial Completion: June 2015
Final Report Submission: December 2015

1664-3 Deferred pediatric study under PREA for the prevention of postoperative nausea and vomiting (PONV) in pediatric surgical patients ages 0 to <17 years. A PK and safety study to characterize the pharmacokinetics of Zuplenz (ondansetron) oral soluble film in pediatric surgical patients ages 0 to <17 years. An age-appropriate formulation must be developed for younger pediatric patients.

Final Protocol Submission: June 2011
Study/Trial Completion: June 2012
Final Report Submission: December 2012

1664-4 Deferred pediatric study under PREA for the prevention of PONV in pediatric surgical patients ages 0 to <17 years. An adequately powered, well-controlled, and randomized dose-response study to evaluate the safety and efficacy of Zuplenz (ondansetron) oral soluble film compared to standard therapy in pediatric surgical patients ages 0 to <17 years. An age-appropriate formulation must be developed for younger pediatric patients.

Final Protocol Submission: December 2016
Study/Trial Completion: December 2017
Final Report Submission: June 2018

Submit final study reports to this NDA. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated “**Required Pediatric Assessment(s)**”.

This product is appropriately labeled for use in ages 4 to 17 years for the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy. Therefore, no additional studies are needed in this pediatric group.

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
Division of Drug Marketing, Advertising, and Communications
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 Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

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 Jagjit Grewal, Regulatory Project Manager, at (301) 796-0846.

Sincerely,

{See appended electronic signature page}

Donna Griebel, M.D.
Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosures: Content of Labeling
Carton and Container Labeling

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22524

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

/s/

DONNA J GRIEBEL

07/02/2010