

# CENTER FOR DRUG EVALUATION AND RESEARCH

## Approval Package for:

### *APPLICATION NUMBER:*

**203856Orig1s000**

*Trade Name:* cyclophosphamide capsules

*Generic Name:* cyclophosphamide capsules

*Sponsor:* Roxane Laboratories, Inc.

*Approval Date:* September 16, 2013

*Indications:* Malignant Diseases: Cyclophosphamide Capsules are indicated for the treatment of: malignant lymphomas (Stages III and IV of the Ann Arbor staging system), Hodgkin's disease, lymphocytic lymphoma (nodular or diffuse), mixed-cell type lymphoma, histiocytic lymphoma, Burkitt's lymphoma; multiple myeloma; leukemias: chronic lymphocytic leukemia, chronic granulocytic leukemia (it is usually ineffective in acute blastic crisis), acute myelogenous and monocytic leukemia, acute lymphoblastic (stem-cell) leukemia (cyclophosphamide given during remission is effective in prolonging its duration); mycosis fungoides (advanced disease); neuroblastoma (disseminated disease); adenocarcinoma of the ovary; retinoblastoma; carcinoma of the breast; Treatment of moderate to severe vasomotor symptoms associated with menopause and prevention of postmenopausal osteoporosis; Minimal Change Nephrotic Syndrome in Pediatric Patients: Cyclophosphamide is indicated for the treatment of biopsy proven minimal change nephrotic syndrome in pediatric patients who failed to adequately respond to or are unable to tolerate adrenocorticosteroid therapy.

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## 203856Orig1s000

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RESEARCH**

*APPLICATION NUMBER:*

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**APPROVAL LETTER**



NDA 203856

**NDA APPROVAL**

Roxane Laboratories, Inc.  
Attention: Anton Amann, Ph.D.  
Executive Director, Drug Regulatory and Medical Affairs  
1809 Wilson Road  
Columbus, OH 43228

Dear Dr. Amann:

Please refer to your New Drug Application (NDA) dated July 3, 2012, received July 3, 2012, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Cyclophosphamide Capsules, 25 mg and 50 mg.

We acknowledge receipt of your amendments dated July 17, 2013; July 29, 2013; August 8, 2013; August 19, 2013; August 26, 2013; August 30, 2013; September 5, 2013 and September 12, 2013.

The July 17, 2013, submission constituted a complete response to our May 3, 2013, action letter.

This new drug application provides for the use of Cyclophosphamide Capsules, 25 mg and 50 mg for the following indications:

Malignant Diseases:

Cyclophosphamide Capsules are indicated for the treatment of:

- malignant lymphomas (Stages III and IV of the Ann Arbor staging system), Hodgkin's disease, lymphocytic lymphoma (nodular or diffuse), mixed-cell type lymphoma, histiocytic lymphoma, Burkitt's lymphoma
- multiple myeloma
- leukemias: chronic lymphocytic leukemia, chronic granulocytic leukemia (it is usually ineffective in acute blastic crisis), acute myelogenous and monocytic leukemia, acute lymphoblastic (stem-cell) leukemia (cyclophosphamide given during remission is effective in prolonging its duration)
- mycosis fungoides (advanced disease)
- neuroblastoma (disseminated disease)
- adenocarcinoma of the ovary
- retinoblastoma
- carcinoma of the breast

Cyclophosphamide, although effective alone in susceptible malignancies, is more frequently used concurrently or sequentially with other antineoplastic drugs.

#### Minimal Change Nephrotic Syndrome in Pediatric Patients:

Cyclophosphamide is indicated for the treatment of biopsy proven minimal change nephrotic syndrome in pediatric patients who failed to adequately respond to or are unable to tolerate adrenocorticosteroid therapy.

#### Limitations of Use:

The safety and effectiveness for the treatment of nephrotic syndrome in adults or other renal disease has not been established.

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.

#### Expiry Dating:

A 24-month expiration dating period is granted for Cyclophosphamide Capsules, 25 mg and 50 mg in the proposed commercial container closure system when stored at 20°C to 25°C (68°F to 77°F), excursion permitted between 15°C and 30°C (between 59°F and 86°F).

### **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). 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 August 30, 2013, submission containing final printed container labels.

### **PROPRIETARY NAME**

If you intend to have a proprietary name for this product, the name and its use in the labels must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit a request for a proposed proprietary name review. (See the guidance for industry *Contents of a*

*Complete Submission for the Evaluation of Proprietary Names*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075068.pdf> and “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012”.)

### **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.

Because none of these criteria apply to your application, you are exempt from this requirement.

### **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>.

### **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 Frank Cross, Jr., Senior Regulatory Health Project Manager, at (301) 796-0876.

Sincerely,

*{See appended electronic signature page}*

Amna Ibrahim, M.D.  
Deputy Director  
Division of Oncology Products 1  
Office of Hematology and Oncology Products  
Center for Drug Evaluation and Research

Enclosures:

Content of Labeling  
Container Labeling

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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.**  
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/s/  
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AMNA IBRAHIM  
09/16/2013