

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

204824Orig2s000

Trade Name: Otrexup Injection (10 mg/0.4 mL, 15 mg/0.4 mL, 20 mg/0.4 mL, and 25 mg/0.4 mL)..

Generic Name: Methotrexate

Sponsor: Antares Pharma, Inc..

Approval Date: October 11, 2013

Indications: Symptomatic control of severe, recalcitrant, disabling psoriasis in adults who are not adequately responsive to other forms of therapy

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APPLICATION NUMBER:

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APPROVAL LETTER



NDA 204824/Original 1
NDA 204824/Original 2

NDA APPROVAL

Antares Pharma, Inc.
100 Princeton South Corporation Center
Suite 300
Ewing, NJ 08628

Attention: Susan Thornton
Senior Director, Regulatory Affairs

Dear Ms. Thornton:

Please refer to your New Drug Application (NDA) dated December 14, 2012, received December 14, 2012, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Otrexup (methotrexate) Injection 10 mg/0.4 mL, 15 mg/0.4 mL, 20 mg/ 0.4 mL and 25 mg/0.4 mL.

We acknowledge receipt of your amendments dated December 19, 2012, and January 25, March 12 and 14, April 8 and 10, May 7, 17, and 23, June 4, 6, 7, 19, and 20, July 22, August 9, September 3 and 12, October 2, 7, 10, and October 11, 2013.

NDA 204824 provides for the use of Otrexup (methotrexate) Injection for the following indications which, for administrative purposes, we have designated as follows:

- NDA 204824/Original 1 – Severe Rheumatoid Arthritis (RA) including polyarticular Juvenile Idiopathic Arthritis (pJIA)
- NDA 204824/Original 2 – Symptomatic control of severe, recalcitrant, disabling psoriasis in adults who are not adequately responsive to other forms of therapy

The subject of this action letter is NDA 204824/Original 1 and NDA 204824/Original 2.

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 package insert, text for the Patient Information Leaflet, and text for the Instructions for Use). 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 container labels that are identical to the enclosed carton and immediate container labels submitted on October 11, 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 titled “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 204824.**” 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.

NDA 204824/Original 1

We are waiving the pediatric study requirement for ages 0 through 2 years because pJIA is extremely rare in this age group and studies would be impossible or highly impractical.

This product is appropriately labeled for use in pJIA patients ages 2 to 17 years. Therefore, no additional studies are needed in this pediatric group.

NDA 204824/Original 2

We are waiving the pediatric study requirement for this application for the psoriasis indication because there is evidence strongly suggesting that the benefit for this drug product do not outweigh the risk in all pediatric age groups.

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 (OPDP)
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 Sadaf Nabavian, Regulatory Project Manager, at (301) 796-2777.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary, Allergy, and
Rheumatology Products
Office of Drug Evaluation II
Center of Drug Evaluation and Research

{See appended electronic signature page}

Tatiana Oussova, M.D., M.P.H.
Deputy Director for Safety
Division of Dermatology and Dental Products
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 and this page is the manifestation of the electronic signature.

/s/

SARAH K YIM
10/11/2013
Signing for Badrul Chowdhury, M.D., Ph.D.

TATIANA OUSSOVA
10/11/2013