DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDAs 088617/S-043 (10 mg)
088618/S-043 (25 mg)
088619/S-044 (50 mg)

**SUPPLEMENT APPROVALS**

Teva Pharmaceuticals USA
U.S. Agent for Pliva Hrvatska d.o.o.
425 Privet Road
Horsham, PA 19044

Attention: Scott Tomsky
Vice President, RA, NA Generics

Dear Mr. Tomsky:

Please refer to your supplemental Abbreviated New Drug Applications (sANDAs) dated and received May 9, 2014, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Hydroxyzine Hydrochloride Tablets USP, 10 mg, 25 mg, and 50 mg.

We also refer to our letter dated April 10, 2014, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for hydroxyzine hydrochloride tablets. This information describes the risk of use of hydroxyzine hydrochloride tablets and fixed drug eruptions as well as cross-sensitivity between hydroxyzine hydrochloride tablets and cetirizine hydrochloride, and between cetirizine hydrochloride and levocetirizine hydrochloride, based on new safety information about this risk identified since the product was approved.

These supplemental new drug applications provide for revisions to the labeling for Hydroxyzine Hydrochloride Tablets, USP consistent with our letter dated April 10, 2014.

We have completed our review of these supplemental applications. They are approved, effective on the date of this letter. However, please make the following post approval revisions to the insert labeling:

ADVERSE REACTIONS:

1. Please relocate the new safety information to appear after the "Psychiatric" subsection.
2. Revise the "Skin and Appendages" subsection in the ADVERSE REACTIONS section to the following:

   Skin and Appendages: Oral hydroxyzine hydrochloride is associated with fixed drug eruptions in postmarketing reports.
   Pruritus, rash, urticaria.

These changes may be made at the time of next printing and submitted in a CBE-0 supplement.

## 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 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), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for these ANDAs, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submissions, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

## PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) 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

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html;

instructions are provided on 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.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in these supplements, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

**REPORTING REQUIREMENTS**

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

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dose forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

If you have any questions, contact Jasmeet Kalsi, Regulatory Project Manager, at 240-402-8977 or jasmeet.kalsi@fda.hhs.gov.

Sincerely,

*{See appended electronic signature page}*

Kathleen Uhl, M.D.
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Enclosure(s):
Content of 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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ROBERT L WEST

06/05/2014

Deputy Director, Office of Generic Drugs, for
Kathleen Uhl, M.D.