DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 091433

Roxane Laboratories, Inc.
Attention: Elizabeth Ernst
Executive Director, Drug Regulatory
Affairs and Medical Affairs
1809 Wilson Road
Columbus, OH 43228

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated March 24, 2009, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Doxercalciferol Capsules, 0.5 mcg, 1 mcg, and 2.5 mcg.

Reference is made to your amendments dated November 20, and December 2, 2009; February 11, May 28, and September 15, 2010; and February 18, March 1, June 17, September 19, September 20, September 21, and September 22, 2011.

We have completed the review of this ANDA, and based upon the information you have presented to date we have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, we are unable to grant final approval to your Doxercalciferol Capsules, 1 mcg and 2.5 mcg, at this time because of the patent issue noted below. Therefore, only your Doxercalciferol Capsules, 0.5 mcg, is **approved**. Your Doxercalciferol Capsules, 1 mcg and 2.5 mcg, are **tentatively approved**.

The reference listed drug (RLD) upon which you have based your ANDA, Hectorol Capsules of Genzyme Corporation, is subject to periods of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent Nos.

5,602,116[1] (the '116 patent) and 6,903,083 (the '083 patent) are scheduled to expire on February 11, 2014, and July 18, 2021, respectively.

With respect to each of these patents, your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that each patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Doxercalciferol Capsules, 0.5 mcg, 1 mcg, and 2.5 mcg, under this ANDA. You have notified the agency that Roxane Laboratories, Inc. (Roxane) complied with the requirements of section 505(j)(2)(B) of the Act, and litigation for infringement of the '116 patent was brought against Roxane within the statutory 45-day period[2] in the United States District Court for the District of Delaware [Genzyme Corporation v. Roxane Laboratories, Inc., Civil Action Nos. 09-cv-00567-GMS and 10-cv-00627].

I. Approval of Doxercalciferol Capsules, 0.5 mcg (Original #1)

With respect to your Doxercalciferol Capsules, 0.5 mcg, we have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, your Doxercalciferol Capsules, 0.5 mcg, is **approved**, effective on the date of this letter. The Division of Bioequivalence has determined your Doxercalciferol Capsules, 0.5 mcg, to be bioequivalent and, therefore, therapeutically equivalent to the RLD, Hectorol Capsules, 0.5 mcg, of Genzyme Corporation. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA.

With respect to 180-day generic drug exclusivity, we note that Roxane was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification for Doxercalciferol Capsules, 0.5 mcg. Therefore, with this approval, Roxane is eligible for 180 days of generic drug exclusivity for Doxercalciferol Capsules, 0.5 mcg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act, will begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv).

[1] The agency notes that the '116 patent was not listed in the Orange Book for the 0.5 mcg strength when you submitted your ANDA, and following its listing for this strength, your paragraph IV certification was submitted in an amendment to your ANDA. Your paragraph IV certifications to the '116 patent for the other two strengths were submitted in your original ANDA.
[2] This period pertains only to the 1 mcg and 2.5 mcg strengths.

Please submit correspondence to this ANDA informing the agency of the date the exclusivity begins to run.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly 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

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

As soon as possible, but no later than 14 days from the date of this letter, submit, using 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 in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). 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/U_CM072392.pdf. The SPL will be accessible via publicly available labeling repositories.

II. Tentative Approval of Doxercalciferol Capsules, 1 mcg and 2.5 mcg (Original #2)

As noted above, your Doxercalciferol Capsules, 1 mcg and 2.5 mcg, are **tentatively approved**. This determination is based upon information available to the agency at this time (i.e., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacturing and testing of the drug product) and is therefore subject to change on the basis of new information that may come to our attention. With respect to these strengths, this letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the Act.

Therefore, final approval cannot be granted until:

1. a. the expiration of the 30-month period provided for in section 505(j)(5)(B)(iii),

   b. the date the court decides[1] that the '116 patent is invalid or not infringed (see sections 505(j)(5)(B)(iii)(I), (II), and (III) of the Act), or

   c. the '116 patent has expired, and

2. The agency is assured there is no new information that would affect whether final approval should be granted.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

To reactivate your ANDA prior to final approval of your Doxercalciferol Capsules, 1 mcg and 2.5 mcg, please submit a ***"MINOR AMENDMENT TO ORIGINAL #2 – FINAL APPROVAL REQUESTED"*** 90 days prior to the date you believe that your Doxercalciferol Capsules, 1 mcg and 2.5 mcg will be eligible for final approval. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, or a settlement or licensing agreement, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, i.e., updated information such as final-printed labeling, chemistry,

manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a ***MINOR AMENDMENT TO ORIGINAL #2 – FINAL APPROVAL REQUESTED***.

In addition to the amendment requested above, the agency may request at any time prior to the date of final approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your ANDA, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in the status of the manufacturing and testing facilities' cGMPs are subject to agency review before final approval of the ANDA will be made. Such changes should be categorized as representing either "major" or "minor" changes to ***ORIGINAL #2,*** and they will be reviewed according to OGD policy in effect at the time of receipt. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

Your Doxercalciferol Capsules, 1 mcg and 2.5 mcg, may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the Act. Also, until the agency issues the final approval letter, this drug product will not be deemed to be approved for marketing under section 505 of the Act, and will not be listed in the "Orange Book."

For further information on the status of this ANDA, or prior to submitting additional amendments, please contact Benjamin Danso, Pharm.D, Product Quality Regulatory Project Manager, at (240) 276-8527.

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

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

/s/

ROBERT L WEST

09/23/2011

Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.