DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-818/S-042

Enzon Pharmaceuticals, Inc.
Attention: Thomas Eckhardt, Dr.sc.nat.
Vice President, Regulatory Affairs
685 US Highway, Route 202/206
Bridgewater, NJ 08807

Dear Dr. Eckhardt:

Please refer to your supplemental new drug application dated March 26, 2008, received March 27, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Adagen® (pegademase bovine) Injection, 250 units/mL.

We acknowledge receipt of your submissions dated May 9, 2008 and August 26, 2008.

This supplemental new drug application provides for the following labeling changes to the Package Insert (Underlined text = addition, ~~Strikethrough text~~ = deletion):

1. In the **PRECAUTIONS/Laboratory Tests** subsection, the sixth paragraph is revised as follows**:**

   Once effective ADA plasma levels have been established, should a patient's plasma ADA activity level fall below 10 μmol/hr/mL (which cannot be attributed to improper dosing, sample handling or antibody development) then ~~all~~ the patient~~s~~ receiving this lot of **ADAGEN®** (pegademase bovine) Injection ~~will be required~~ should be requested to have a blood sample for plasma ADA determination taken prior to their next injection of **ADAGEN®** (pegademase bovine) Injection. ~~The index patient will require re-testing for determination of plasma ADA activity prior to his/her next injection of **ADAGEN®** (pegademase bovine) Injection. If this value, as well as the value from one of the other patients from a different site, is less than 10 μmol/hr/mL then the lot in use will be recalled and replaced with a new clinical lot by ENZON Pharmaceuticals, Inc.~~

2. In the **ADVERSE REACTIONS** section, the first paragraph is revised as follows:

   Clinical experience with ADAGEN® (pegademase bovine) Injection has been limited. The following adverse reactions were ~~have been~~ reported during clinical trials: headache in one patient and pain at the injection site in two patients.

3. In the **ADVERSE REACTIONS** section, a second, third, and fourth paragraphs are added as follows:

   The following adverse reactions have been identified during post-approval use of ADAGEN® (pegademase bovine) Injection. Because these reactions are reported voluntarily from a very small population, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

   Hematologic events: hemolytic anemia, auto-immune hemolytic anemia, thrombocythemia

   Dermatological events: injection site erythema, urticaria

We completed our review of this supplemental application as amended. This supplemental application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text submitted March 26, 2008.

Submit revised content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text. Upon receipt and verification, we will transmit that version to the National Library of Medicine for posting on the DailyMed website.

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, please call Christina H. Chi, PH.D., Regulatory Health Project Manager, at (301) 301-796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Package Insert

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

/s/

Renata Albrecht

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