

ANDA 75-243

August 31, 1999

ESI Lederle, Inc.
Attention: J. Barton Kalis
2 Esterbrook Lane
Cherry Hill, NJ 08003-4099

Dear Sir:

This is in reference to your abbreviated new drug application dated November 4, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Midazolam Hydrochloride Injection, 1 mg (base)/mL [packaged in 2 mL, 5mL, and 10 mL vials], and 5 mg (base)/mL [packaged in 1 mL, 2mL and 10 mL vials].

Reference is also made to your amendments dated September 29, 1998; and April 30, May 7, May 14, July 15, and August 25, 1999.

We have completed the review of this abbreviated application and have concluded that based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Therefore, the application is **tentatively approved**. This determination is based upon information available to the Agency at this time, (i.e., information in your application and the status of current good manufacturing practices (CGMP) of the facilities used in the manufacture and testing of the drug product), and is subject to change on the basis of new information that may come to our attention. Your application cites Versed Injection of Hoffmann LaRoche, Inc. (Roche) as the reference listed drug product (RLD) upon which you have based your application. Versed Injection of Roche is subject to a period of patent protection which was subsequently extended with an additional 6-month period of market exclusivity. As noted in the agency's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations", the patent protection (U.S. Patent No. 4,280,957) was to have expired on December 20, 1999. However, this period was extended under Section 111 of the Food and Drug Administration Modernization Act (FDAMA) [(21 U.S.C. 355a (1997))]

for an additional period of 6 months. Therefore, final approval of your application may not be made effective pursuant to 21 U.S.C. 355(j)(4)(B)(ii) of the Act until that period has expired, i.e., June 20, 2000.

Because the agency is granting a tentative approval to this application, please submit an amendment at least 60 days (but not more than 90 days) prior to the date you believe your application will be eligible for final approval. This amendment should identify changes, if any, in the conditions under which the product was tentatively approved, and should include updated information such as final printed labeling, chemistry, manufacturing, and/or controls data as appropriate. An amendment should be submitted even if none of these changes were made. This amendment should be designated clearly in your cover letter as a MINOR AMENDMENT. In addition to this amendment, the Agency may request at any time prior to the final date of approval that you submit an additional amendment containing the information described above.

Failure to submit either, or if requested both amendments may result in rescission of the tentative approval status of your application, may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this abbreviated application, as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (CGMPs) are subject to agency review before final approval of the application will be made.

The drug product that is the subject of this abbreviated application 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 501 of the Act. Also, until the agency issues the final approval letter, your drug product will not be deemed approved for marketing under 21 U.S.C. 355 and will not be listed in the "Approved Drug Products with Therapeutic Equivalence Evaluations" list, (the

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"Orange Book"), published by the Agency. Should you believe that there are grounds for issuing the final approval letter prior to June 20, 2000, you should amend your application accordingly.

At the time you submit any amendments, please contact Kassandra Sherrod, Project Manager, at (301) 827B5849, for further instructions.

Sincerely yours,

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research