ANDA 75-527 March 31, 2000

Invamed Inc.
Attention: Mahendra Patel, Ph.D.
2400 Route 130 North
Dayton, NJ 08810

Dear Sir:

This is in reference to your abbreviated new drug application dated December 18, 1998, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Bisoprolol Fumarate and Hydrochlorothiazide Tablets, 2.5 mg/6.25 mg,
5 mg/6.25 mg, and 10 mg/6.25 mg.

Reference is also made to your amendments dated August 13, 1999; and February 28, 2000.

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 (CGMPs) 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.

The reference listed drug product (RLD) upon which you have based your application, Ziac® Tablets of Lederle Laboratories (Lederle), is subject to a period of patent protection (U.S. Patent No. 4,258,062, the '062 patent). Your application contains a Paragraph III Certification to the '062 patent under Section 505(j)(2)(A)(vii)(III) of the Act stating that you will not market this drug product prior to the expiration of this patent, which was due to expire on March 24, 2000. However, Section 111 of Title I of the Food and Drug Administration Modernization Act of 1997 (the Modernization

Act) created section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a). Section 505A permits certain applications to obtain an additional six months of marketing exclusivity (pediatric exclusivity) if, in accordance with the requirements of the statute, the sponsor of the RLD submits data previously requested by the Agency relating to the use of the drug in the pediatric population.

The holder of the RLD has made such a submission to the agency. The length of this additional exclusivity is to be determined within 90 days by the agency's Pediatric Exclusivity Board located in the Office of Review Management (ORM). The additional exclusivity, if granted for the maximum period, would add 6 months of additional exclusivity beyond the expiration of the '062 patent. OGD will closely monitor the board's progress with respect to the granting of pediatric exclusivity. You will be informed of the board's decision by the project manager. Therefore, final approval of your application may not be made effective pursuant to 21 U.S.C. 355(j)(5)(D) of the Act until the additional period of market exclusivity granted to Lederle has expired, i.e., potentially September 24, 2000.

Because the Agency is granting a tentative approval for this application, please submit an amendment at least 60 days (but not greater 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 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 date of final 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, or 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.

Please note that this drug product 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 and 21 U.S.C. 331(d). Also, until the Agency issues the final approval letter, this 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 "Orange Book"), published by the Agency. Should you believe that there are grounds for issuing the final approval letter prior to September 24, 2000, you should amend your application accordingly.

At the time you submit any amendments, you should contact Timothy Ames, Project Manager, at (301) 827–5798, for further instructions.

Sincerely yours,

Gary Buehler
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research