ANDA 75-166

October 7, 1999

Brightstone Pharma, Inc.
Attention: Steven Jensen
10450 Science Center Drive
San Diego, CA 92121

Dear Sir:

This is in reference to your abbreviated new drug application dated July 10, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Isosorbide Mononitrate Extended-release Tablets, 60 mg.

Reference is also made to your amendments dated February 27, 1998; March 26, June 4, August 27, September 20, and October 4, 1999.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Isosorbide Mononitrate Extended-release Tablets, 60 mg, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Imdur**7** Extended-release Tablets, 60 mg, of the Schering Corporation).

Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application. The Ainterim@ dissolution test and tolerances are:

> The dissolution testing should be conducted in 100 mL of water, at 37^{o}C using USP Apparatus 2 (paddle) at 50 rpm. The test product should meet the following specifications:
>
> > [----------] and [--------] of the labeled amount of the drug in the dosage form are dissolved in 1 hour, 2 hours, 4 hours, 7 hours, and 10 hours, respectively.

The Ainterim@ dissolution test and tolerances should be finalized by submitting dissolution data for the first three production

size batches in a supplemental application. The supplemental application should be submitted under 21 CFR 314.70(c)(1) when there are no revisions to the Ainterim@ specifications or when the final specifications are tighter than the Ainterim@ specifications. In all other instances the supplement should be submitted under 21 CFR 314.70(b)(2)(ii).

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application 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.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Validation of the regulatory methods has not been completed. It is the policy of the Office not to withhold approval until the validation is complete. We acknowledge your commitment to satisfactorily resolve any deficiencies which may be identified.

Sincerely yours,

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