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APPROVAL PACKAGE FOR:

APPLICATION NUMBER
19-032/S-016 and S-017

Approval Letter

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-032/ S-016
S-017

A. H. Robbins
Attention: Ms. Diane Mitrione
150 B/3 North Radnor Chester Road
St. Davids, PA 19087

Dear Ms. Mitrione:

Please refer to your supplemental new drug applications dated August 24, 2000 (S-016) and November 20, 2000 (S-017) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tenex (guanfacine hydrochloride) 1 and 2 mg Tablets.

We acknowledge receipt of your submission dated October 31, 2001. This submission constitutes a complete response to our February 23, 2001 (S-016) and April 20, 2001 (S-017) approvable letters.

These supplemental new drug applications provide for final printed labeling revised as follows:

S-016

Added **PRECAUTIONS/Geriatric Use**

Clinical studies of Tenex did not include sufficient numbers of subjects aged 65 and over to determine whether they responded differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy (see **CLINICAL PHARMACOLOGY-Pharmacokinetics**).

S-017

Addition to the **PRECAUTIONS/Pediatric Use** section:

There have been spontaneous postmarketing reports of mania and aggressive behavioral changes in pediatric patients with attention-deficit hyperactivity disorder (ADHD) receiving Tenex. The reported cases were from a single center. All patients have medical or family risk factors for bipolar disorder. All patients recovered upon discontinuation of guanfacine HCl.

We also noted minor editorial changes.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text and with the minor editorial revisions listed below. Accordingly, these supplemental applications are approved effective on the date of this letter.

At the time of the next printing of the labeling, please make the following correction to the **PRECAUTIONS/Pediatric Use** section:

- In the next to the last sentence, change the word have to had.
- The sentence should read:
  All patients had medical or family risk factors for bipolar disorder.

This change should be reported in your next annual report.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call:

Mr. Daryl Allis
Regulatory Health Project Manager
(301) 594-5309

Sincerely,

/S/
{See appended electronic signature page}

Douglas C. Throckmorton, M.D.
Acting Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
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/

Doug Throckmorton
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