NDA 12-342/SLR-037/039/040/044/046/048/051

SmithKline Beecham
Attention: Eloise Scott, D.V.M.
Associate Director, Regulatory Affairs
1250 S. Collegeville Road
P.O. Box 5089
Collegeville, PA 19426-0989

15 MAR 2001

Dear Dr. Scott:

Please refer to your supplemental new drug applications dated July 8, 1988 (S-037), September 28, 1988 (S-039), April 14, 1989 (S-040), June 13, 1990 (S-044), September 25, 1990 (S-046), May 13, 1992 (S-048), and November 26, 1996 (S-051), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Parnate (tranylcypromine sulfate) 10 mg Tablets.

Reference is also made to an Agency letter dated May 9, 1991, informing you that supplemental applications 037, 039, 040, 044, and 046 were permissible, and requesting specific changes to the labeling.

We additionally refer to Agency letters dated October 21, 1987, June 8, 1988, and June 27, 1996, requesting revisions to the Parnate labeling.

These supplemental applications provide for the following revisions to the Parnate labeling:

S-037

1. Under **CONTRAINDICATIONS**:

    a. The deletion of the restriction that Parnate be withheld from patients over 60 years of age.

    b. The expansion of the interaction between Parnate and tryptophan in response to an Agency letter dated October 21, 1987.

2. Under **CONTRAINDICATION**, **OTHER PRECAUTIONS**, and **DOSAGE and ADMINISTRATION**:

    The deletion of the statements that withdrawal from Parnate should be gradual.

S-039

1. Under **DESCRIPTION**:

   The addition of an inactive ingredient, FD&C Yellow No. 6.

2. Under **SUMMARY OF CONTRAINDICATIONS** and **CONTRAINDICATIONS**:

   The addition of dextromethorphan as a contraindication in response to an Agency letter dated October 21, 1987.

3. Under **CONTRAINDICATIONS**:

   a. The addition of a paragraph to warn about concomitant use of fluoxetine.

   b. Under the subsection **Foods with High Tyramine Content**, after the word "beer", the addition of the phrase "(including non-alcoholic beer)" in response to an Agency letter dated June 8, 1988. You also added "caviar" to this food list.

   c. The revision of the phrase "neuroleptic and behavioral" to "neurologic and behavioral" in response to an Agency letter dated September 14, 1988.

S-040

The addition of "clomipramine hydrochloride Anafranil (Ciba-Geigy)" into **CONTRAINDICATIONS** section 3, subsection **In combination with MAO inhibitors or with dibenzazepine-related entities**.

S-044

The addition of "sauerkraut" under the subsection **Foods with High Tyramine Content** of the **CONTRAINDICATIONS** section.

S-046

The revision of the **DESCRIPTION** section to delete those ingredients used in the sugar-coated tablet and include those in the aqueous, film-coated tablet formulation.

S-048

The supplement provides for revisions as requested in the Agency permissible letter dated May 5, 1991. The specific changes are as follows:

1. The subsection **In Combination with Fluoxetine** under the **CONTRAINDICATIONS** section has been retitled **In Combination with Selective Serotonin Reuptake Inhibitors**. Additionally, this section was reworded as requested in the Agency letter dated May 9, 1991.

2. All references to Parnate being contraindicated in patients over 60 years old have been deleted. However, a paragraph in the **PRECAUTIONS** section that Parnate should be used with caution in older patients has been added.

3. A **Post-Introduction Reports** subsection under the **ADVERSE REACTIONS** section has been added.

S-051

1. The addition of a new subsection under the **CONTRAINDICATIONS** section entitled **In Combination with Dexfenfluramine Hydrochloride**. We note that this addition was requested in an Agency letter dated June 27, 1996.

2. Several minor editorial changes including the reformatting of the inactive ingredients so that they are in alphabetical order have been made.

We have completed the review of these supplemental applications 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 submitted final printed labeling (package insert submitted November 26, 1996-Label Code PT:L61), which incorporates the revisions listed above. Accordingly, these supplemental applications are approved effective on the date of this letter.

Labeling changes of the kind which you have proposed under the above supplemental applications are permitted by section 314.70(c) of the regulations to be instituted prior to approval of the supplement. It is understood that the changes, described in the above NDA supplements, have been made.

However, we note that your most current labeling, Label Code PT:L61, does not incorporate the expansion of the interaction between Parnate and tryptophan as submitted under S-037 and as requested in an Agency letter dated October 21, 1987. Therefore, we request, at your next printing of final printed labeling, that this change be incorporated into product labeling.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" 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, call Mr. Paul David, R.Ph., Senior Regulatory Project Manager, at (301) 594-5530.

Sincerely,

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research