HFD-104

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville MD 20857

NDA 20-031
NDA 20-710

FEB 28 2000

SmithKline Beecham Pharmaceuticals
Attention: Thomas F. Kline
Manager, U.S. Regulatory Affairs
1250 South Collegeville Road, P.O. Box 5089
Collegeville, Pennsylvania 19426-0989

Dear Mr. Kline:

Please refer to your New Drug Applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Paxil (paroxetine hydrochloride) 10 mg, 20 mg, 30 mg, and 40 mg tablets (NDA 20-031) and 10 mg/5 ml oral suspension (NDA 20-710).

We additionally refer to an Agency pediatric Written Request letter dated April 28, 1999.

We acknowledge receipt of your submission dated December 13, 1999, providing for proposed changes in the Written Request for pediatric studies.

We have reviewed your proposed changes and are amending the below listed sections of the Written Request. All other terms stated in our Written Request issued on April 28, 1999, remain the same.

- **Pediatric Depression: Study Design – Pediatric Efficacy and Safety Studies**

  We are amending this section to add the following: "One study for depression may include only adolescents (ages 12 –17). If only adolescents are studied in one of the two required depression studies, then the other depression study must include either children (ages 7-11) or both children and adolescents (ages 7-17)."

  We are additionally amending this section of the Written Request to delete "Randomization must be stratified by the two age groups studied" and add "We recommend stratifying randomization by the two age groups studied. If this is not done, then recruitment should be adjusted so that at least 40% of each age group is represented in the studies which include children and adolescents."

- **Pediatric Obsessive Compulsive Disorder (OCD): Study Design – Pediatric Efficacy and Safety Studies**

  We are amending this section of the Written Request to delete "Randomization must be stratified by the two age groups studied" and add "We recommend stratifying randomization by the two age groups studied. If this is not done, then recruitment should be adjusted so that at least 40% of each age group is represented in the study which includes children and adolescents."

- **Pediatric Depression/Obsessive Compulsive Disorder (OCD): Study Evaluations – Pediatric Pharmacokinetic Study**

  We are amending this section for both depression and OCD as follows:

  "The pharmacokinetic assessments should be made with respect to the study drug and any metabolites that make substantial contributions to its efficacy and/or toxicity. For the parent and each metabolite followed, the data collected should provide estimates of the pharmacokinetic *parameters ~~including~~ such as AUC, half-life,* C_{max}, t_{max}, *and apparent oral clearance in pediatric* subjects in the relevant age range. You should be aware that a draft guidance document on pediatric pharmacokinetic studies is available under [www.fda.gov/cder/guidance/index.htm, under Clinical/Pharmacological (Draft)].

  Additionally, one pharmacokinetic study would suffice for both indications."

Your other proposed changes to the Written Request (b) (4) have not been accepted and are not terms of the Written Request.

(b) (4)

Reports of the studies that meet the terms of the Written Request dated April 28, 1999, as amended by this letter must be submitted to the Agency (b) (4)

Reports of the studies should be submitted as a supplement to your approved NDA with the proposed labeling changes you believe would be warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission **"SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED"** in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, MD 20855-2773.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked **"PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font. bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits to the pediatric population.

If you have any questions, call Paul A. David, Regulatory Project Manager, at (301) 594-5530.

Sincerely yours,

RB for RT 2/28/00

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Archival NDAs 20-031 & 20-710
HFD-120/Div Files
HFD-100/RTemple
HFD-120/PDavid
HFD-120/RKatz/TLaughren/AMosholder/RGlass
HFD-600/Office of Generic Drugs
HFD-2/MLumpkin
HFD-104/DMurphy
2/23/00
filename: PAXIL\AMENDED PEDIATRIC WR 12-13-99.DOC

PEDIATRIC WRITTEN REQUEST LETTER
INFORMATION REQUEST (IR)