HFD-114
Amend

IND 43,272
NDA 20-626

Glaxo Wellcome Inc.
Attention: Ms. Judith Babo
Five Moore Drive
PO Box 13398
Research Triangle Park, NC 2770

JUN 21 2000

Dear Ms. Babo:

Reference is made to your correspondence dated October 11, 1999 and February 28, 2000 requesting changes to FDA's June 7, 1999 Written Request for pediatric studies for Imitrex (sumatriptan) nasal spray.

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 June 7, 1999 remain the same.

With reference to the adolescent long term safety study (referred to in the original Written Request as "Study 3"), we agree with your February 28, 2000 proposal to demonstrate adequate safety in adolescents who experience two or more migraine headaches per month at study entry.

In particular, the following section of the original June 7, 1999 request is amended as follows.

Original Letter:

Number of patients to be studied or power of the study to be achieved

Study 3: A sufficient number of adolescent migraine patients to be able to characterize the long-term safety of sumatriptan nasal spray when used to treat multiple migraine attacks over one year. Each patient should treat, on average, two or more headaches per month. At a minimum, 300 to 600 patients, using the highest planned marketed dose, should be exposed for six months, and 100 patients, using the highest planned marketed dose, should be exposed for one year.

Entry criteria (i.e., inclusion/exclusion criteria)

Study 2 and 3: Adolescent patients between 12 and 17 years of age, with an average of 1 to 6 International Headache Society (IHS) defined migraine headaches per month. The patients within this age group of 12-17 years old should be approximately evenly distributed.

FDA amendment:

Number of patients to be studied or power of the study to be achieved

Study 3: A sufficient number of adolescent migraine patients to be able to characterize the long-term safety of sumatriptan nasal spray when used to treat multiple migraine attacks over

one year. The study should enroll patients who experience, on average, two or more migraine headaches per month. At a minimum, 300 to 600 patients, using the highest planned marketed dose, should be exposed for six months, and 100 patients, using the highest planned marketed dose, should be exposed for one year.

Entry criteria (i.e., inclusion/exclusion criteria)

Study 2 and 3: Adolescent patients between 12 and 17 years of age, with at least two International Headache Society (IHS) defined migraine headaches per month. The patients within this age group of 12-17 years old should be approximately evenly distributed.

With reference to the pharmacokinetic study (referred to in the original Written Request as "Study 1"), we agree with your October 11, 1999 proposal to allow the use of adult historical control data.

In particular, the following section of the original June 7, 1999 request is amended as follows.

Original letter:

Study design

Study 1: Single dose, parallel group inpatient pharmacokinetic study in adolescents and adults with history of migraine.

FDA amendment:

Study design

Study 1: Single dose, parallel group inpatient pharmacokinetic study in adolescents and adults with history of migraine. Alternatively, a single dose inpatient pharmacokinetic study in adolescents, which compares the results with appropriate adult historical control data, may be substituted.

Reports of the studies that meet the terms of the Written Request dated June 7, 1999, as amended by this letter must be submitted to the Agency on or before July 1, 2002, in order to possibly qualify for pediatric exclusivity extension under Section 505A of the Act.

Please submit protocols for the above studies to an investigational new drug application (IND) and clearly mark your submission, "PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY" in large font, bolded type at the beginning of the cover letter of the submission. Please notify us as soon as possible if you wish to enter into a written agreement by submitting a proposed written agreement. Please clearly mark your submission, "PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES" in large font, bolded type at the beginning of the cover letter of the submission.

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, contact Ms. Lana Chen, Regulatory Project Manager, at (301) 594-5529.

Sincerely yours,

6/21/00

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

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NDA 20-626
~~Page 3~~ cc 6/14/00

cc:
Archival NDA 20-626
IND 43,272

HFD-120/division file
All other INDs/NDAs for the active moiety (same sponsor only): N20-080, N20-132
Revised cc 6/14/00 & 6/19/00
HFD-120/Chen 5/19/00 6/14/00 6/14/00
HFD-120/Katz/Feehey/Oliva/Glass 5/17/00 6/14/00
5/17/00

HFD-101/Temple
HFD-600/Office of Generic Drugs
HFD-2/M.Lumpkin
HFD-104/Peds/D.Murphy
HFD-104/Peds/T.Crescenzi

Drafted by: lyc May 2, 2000
Initialed by:
Final:

filename: wpfiles/imtrx_in/revwrlet.doc

REVISED PEDIATRIC WRITTEN REQUEST LETTER
INFORMATION REQUEST (IR)