HFD 104 Murphy

NDA 20-929

DEC 22 1999

AstraZeneca
725 Chesterbrook Blvd.
Wayne, PA 19087-5677

Attention: Eric Couture, Ph.D.
Director, Regulatory Liaison

Dear Dr. Couture:

Reference is made to your correspondence dated June 16, 1999, requesting changes to FDA's December 14, 1998, Written Request for pediatric studies for budesonide.

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 December 14, 1998, remain the same.

Type of studies:

Study 1: Safety of budesonide nebulizing suspension for treatment of asthma in children between the ages of 6 months and 1 year, with efficacy parameters assessed as secondary endpoints.

Age Group in Which Studies will be Performed:

Study 1: Children between the ages of 6 months and 1 year. Approximately half of the study subjects in each study group must be below 9 months of age. In addition, there must be at least 5 subjects for each of the age groups of $\geq$ 6 months and < 7 months, $\geq$ 7 months and < 8 months, and $\geq$ 8 months and < 9 months in each of the 3 study groups.

Number of Subjects to be Studied:

Study 1: A minimum of 30 subjects per study group (3 groups, 90 subjects) must complete the study.

Entry criteria:

Study 1: Children between the ages of 6 months and one year with asthma who are likely to benefit from inhaled corticosteroids. The subjects should not have received systemic corticosteroids for at least 2 months, and the cumulative dose should not exceed 14 days of 1 mg/kg/day of prednisone, or its equivalent. Subjects who have received inhaled corticosteroids in the past may be recruited; however, they must undergo a minimum 2 -week "washout" prior to entry into the trial. The total daily dose of prior inhaled corticosteroid should not exceed a dose comparable to the maximum dose to be studied in this trial (i.e., 1.0 mg/kg/day of Pulmicort Respules).

Study 2: Children between the ages of 2 and 6 years with rhinitis who may derive benefit from intranasal corticosteroids. The study subjects must not have used any systemic corticosteroids within 90 days of randomization and must not have used inhaled (bronchial or nasal) or topical corticosteroids within 30 days of randomization. Study subjects must be free from other clinically significant medical problems.

Clinical endpoints:

Study 1: Efficacy will be considered a secondary assessment for purposes of this study. At least three efficacy parameters should be assessed and may include asthma symptom scores, use of rescue medications, asthma episodes, and subject discontinuations due to treatment failures. Efficacy evaluations must be made at the start of the study and reassessed every 4 weeks thereafter.

Statistical Information:

Study 1: The safety data should be tabulated and standard summary statistics should be utilized. Efficacy parameters should be evaluated using appropriate analyses, including summary statistics and inferential testing. (However, because of power considerations, a demonstration of statistically significant differences is not expected.)

Labeling that may result from the studies:

Study 1: The appropriate sections may be updated to incorporate the information.

Timeframe:

Full study reports must be submitted to the Agency by June 30, 2001.

Reports of the studies that meet the terms of the Written Request dated December 14, 1998, as amended by this letter must be submitted to the Agency on or before June 30, 2001, 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 new drug application, or an amendment to your pending application, as appropriate, 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 Mrs. Gretchen Trout, Regulatory Project Manager, at 301-827-1058.

Sincerely yours,

John K. Jenkins, M.D., F.C.C.P.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Archival NDAs 20-746 and 20-929
Archival INDs 21,632 and 44,535
HFD-570/division files
HFD-570/Trout
HFD-570/Purucker
HFD-570/Anthracite
HFD-570/Chowdhury
HFD-570/Meyer
HFD-102/Jenkins
HFD-600/Office of Generic Drugs
HFD-2/M.Lumpkin
HFD-104/D.Murphy
HFD-002/T.Crescenzi

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Chowdhury/11-24-99
Meyer/11-24-99

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REVISED PEDIATRIC WRITTEN REQUEST LETTER
INFORMATION REQUEST (IR)