



DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF BIOSTATISTICS

Statistical Review and Evaluation

CLINICAL STUDIES

NDA: 20-548/(b)(4)8-018

Name of drug: Flovent Inhalation Aerosol (Fluticasone Propionate)

Applicant: GlaxoSmithKline

Indication: Maintenance treatment of asthma as prophylactic therapy

Documents reviewed: \\Cdsesub1\n20548\N_000\2002-12-13\clinstat

Project manager: Ladan Jafari

Clinical reviewer: Peter Starke, M.D.

Dates: Received 12/12/02; user fee 6/5/03

Statistical reviewer: Lisa Kammerman, Ph.D.

Statistics team leader: Lisa Kammerman, Ph.D.

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Keywords: NDA review, clinical studies, pediatrics

This supplement contains two pediatric studies (FMS30058 and FMS30059) submitted in response to a written request. The studies have a common design: double-blind, double-dummy, comparing 88 mcg BID, 44 mcg BID and Placebo delivered via MDI with CFC propellants. The first study evaluated children aged 24 to 47 months inclusive; the other evaluated children aged 6 to 23 months inclusive.

Because of concerns with the integrity of the data (see the clinical review for details), an exhaustive statistical review is not being done at this time. The applicant will be asked to clarify the data concerns.

The following general issues need to be considered if further review is warranted:

1. Comparisons of the two study treatment groups with placebo need to be adjusted for multiple comparisons.
2. An analysis of covariance (ANCOVA) model using age, treatment by age interaction, region, and treatment by region interaction needs to be done to reflect the stratification used at the time of randomization. The efficacy analyses in the supplement contained numerous covariates. For the efficacy analyses in Study FMS30058, the ANCOVA models included treatment group, baseline value, age group, holding chamber, sex, region, pre-treatment low-dose CS therapy, family history of asthma and subject history of allergy. For Study FMS30059, the ANCOVA models did not include 'holding chamber'. Because the study evaluated older subjects, the use of a holding chamber was not needed.

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/s/

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5/21/03 08:09:18 PM
BIOMETRICS
Concur with review.