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RESEARCH**

APPLICATION NUMBER:

NDA 21-254

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-254

GlaxoSmithKline
P. O. Box 13398
Five Moore Drive
Research Triangle Park, NC 27709-3398

Attention: Tracy L. Fischer, Pharm.D.
Manager, Regulatory Affairs

Dear Dr. Fischer:

Please refer to your new drug application (NDA) dated December 20, 2000, received December 20, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Advair HFA (fluticasone propionate and salmeterol xinafoate) Inhalation Aerosol.

We acknowledge receipt of your submissions dated February 9, 22, and 23, March 5, 14, 15, and 30, April 20, June 5, 12, 28, and 29, September 4, October 3, 11, and 30, and November 7, 14, and 26, 2001, April 15, and 25, May 15, July 31, August 22, and September 6, and 12, 2002, March 24, 2004, June 7, December 7, 2005, and February 17, April 14, May 2, and 18, and June 6, and 7, 2006.

The December 7, 2005, submission constituted a complete response to our October 16, 2002, action letter.

This new drug applications provides for the use of Advair HFA Inhalation Aerosol for the long-term, twice-daily maintenance treatment of asthma in patients 12 years of age and older.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the submitted labeling (text for the package insert, and the Medication Guide, copy enclosed, submitted on June 6, 2006, and immediate container and carton labels submitted on June 7, 2006). Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission(s) "**FPL for approved NDA 21-254.**" Approval of this submission by FDA is not required before the labeling is used.

We remind you of the following agreements as listed in your submission dated May 18, 2006.

1. Agree that efforts will be made to examine the (b) (4) ----- --and to minimize it if possible, file any associated chan-----provide brief summaries of any progress in annual reports.
2. Agree to re-evaluate the Parametric Tolerance Interval Test approach for dose content uniformity once an adequate database is available (i.e., approximately 18 months after product launch), and (b) (4) -----
3. Agree to submit the (b) (4) -----
(b) (4) -----
4. Agree that the following post-approval agreements and subsequent changes and filing mechanisms outlined in the May 14, 2004, approval letter for the Flovent HFA Inhalation Aerosol application (N21-433) will also apply to the Advair HFA application in cases where there is commonality of the chemistry, manufacturing, and controls.
 - a. (Commitment 1). (b) (4) ----- issues will be addressed for fluticasone propionate and fluticasone propio----- (b) (4), (b) (4) -----
(b) (4) -----
 - b. (Commitment 2). Implementation of a (b) (4) -----
(b) (4) -----, will occur ----- be-
(b) (4) -----

 - c. (Commitment 11). You will submit a prior approval supplement to implement final acceptance criteria for quantitative mass balance within 18 months of product launch.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for ages 0 to less than 4 and deferring pediatric studies for ages greater than 4 to less than 12 years for this application.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the treatment of asthma in pediatric patients ages greater than 4 to less than 12.

Final Report Submission: December 2007.

Submit final study reports to this NDA. For administrative purposes, all submissions related to this/these pediatric postmarketing study commitment(s) must be clearly designated "**Required Pediatric Study Commitments**".

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Ms. Ladan Jafari, Regulatory Project Manager, at (301) 796-1231.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: Pkg insert

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Badrul Chowdhury
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