CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: 20-831

Trade Name: Foradil Aerolizer

Generic Name: formoterol fumarate inhalation powder

Sponsor: Novartis

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APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-831

Novartis Pharmaceuticals Corporation
59 Route 10
East Hanover, New Jersey 07936

Attention: Kathleen Basmadjian, Ph.D.
Assistant Director
Drug Regulatory Affairs

Dear Dr. Basmadjian:

Please refer to your pending new drug application dated June 24, 1997, received June 26, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Foradil Aerolizer (formoterol fumarate inhalation powder).

We acknowledge receipt of your submissions dated August 7, 11, 15, 20, 28, and 29, September 19, and October 16, 24 (2), and 27, 1997, January 30, February 5, 19, and 24, March 17 (2) and 20, May 13 and 14, June 1, October 19, November 10, and December 10, 1998, November 23, 1999, February 16, March 30, April 28, August 17, September 29, and December 1 and 7, 2000, and February 13 and 15, 2001. Your submission of August 17, 2000, constituted a complete response to our May 24, 2000, action letter.

This new drug application provides for the use of Foradil Aerolizer (formoterol fumarate inhalation powder) for long-term, twice daily (morning and evening) administration in the maintenance treatment of asthma and in the prevention of bronchospasm in adults and children 5 years of age and older with reversible obstructive airways disease, including patients with symptoms of nocturnal asthma, who require regular treatment with inhaled, short-acting, $beta_2$-agonists. It is not indicated for patients whose asthma can be managed by occasional use of inhaled, short-acting, $beta_2$-agonists. Foradil Aerolizer is also indicated for the acute prevention of exercise-induced bronchospasm (EIB) in adults and children 12 years of age and older, when administered on an occasional, as-needed basis.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed-upon labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert, patient package insert, and carton labels submitted February 15, 2001, and immediate container labels submitted February 13. 2001). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 20-831." Approval of this submission by FDA is not required before the labeling is used.

As stated in your correspondence dated December 13, 2000, you are reminded of your agreement to report any post-marketing medication error reports, or potential-error reports, as 15-day reports for the first 6 months of the product distribution.

We remind you of your postmarketing study commitment in your submission dated February 9, 2001. This commitment is listed below.

You have committed to conduct a large, simple, placebo-controlled postmarketing study to further evaluate the safety and efficacy of regular, twice-daily administration of one or more dose levels of Foradil Aerolizer above that of the approved dose (12 mcg twice daily), in comparison to the safety and efficacy of the approved dose.

You have committed to the following time-lines for this study:

Protocol Submission:	Within 3 months of the date of this letter
Study Start:	Within 12 months of the date of this letter
Final Report Submission:	Within 30 months of the date of this letter

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments should be prominently labeled **"Postmarketing Study Protocol," "Postmarketing Study Correspondence," or "Postmarketing Study Commitment Final Report."**

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, 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 (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55.

[redacted] However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

We are waving the requirements of the pediatric studies for maintenance treatment of asthma for children up to 5 months of age and for exercise-induced bronchospasm for children up to 3 years of age.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study, Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Pulmonary and Allergy Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Ms. Parinda Jani, Project Manager, at (301) 827-1064.

Sincerely yours,

/S/

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

APPEARS THIS WAY
ON ORIGINAL