DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-861 **NDA APPROVAL**

Alcon Research, Ltd.
6201 South Freeway, R7-18
Fort Worth, TX 76134-2099

Attention: Terry J. Dagnon, Senior Director
Regulatory Affairs

Dear Mr. Dagnon:

Please refer to your new drug application (NDA) dated December 24, 2004, received December 27, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (the FDCA) for Patanase (olopatadine hydrochloride) Nasal Spray.

We acknowledge receipt of your submissions dated February 1, 3, and 9, March 31, April 5, 6, 11, 14, and 25, May 2, 13, and 25, June 27, July 7, 11, 14, 18, and 22, September 2, 13, and 23, October 5, 6, and 27, November 1, 21, and 29, and December 6, 2005, January 10, 12, and 31, February 2, 7, and 21, April 21, May 5, 15, 17, 22, and 31, June 9, and 28, July 17, and 26, and August 4, 2006, July 19, November 14 and 29, and December 7, 13, and 19, 2007, and January 3, 10, and 30, February 4, 21, 25, 26, 27, and 28, and March 4, 6, 13, 19, 21, and 24, 2008.

The September 27, 2007, submission constituted a complete response to our October 27, 2005, action letter.

This new drug application provides for the use of Patanase (olopatadine hydrochloride) Nasal Spray 0.6% for the treatment of symptoms of seasonal allergic rhinitis in patients 12 years of age and older.

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

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to 2 years because necessary studies would be impossible to conduct in light of the fact that seasonal allergic rhinitis does not occur in children under 2 years.

We are deferring pediatric studies for ages 2 to 11 years for this application because the drug product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric study required under section 505B(a) of the FDCA is a required pediatric postmarketing study. The status of this required pediatric postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. This requirement is listed below.

- Deferred pediatric study under PREA for the treatment of allergic rhinitis in pediatric patients ages 2 to 11 years of age.

- Final Report Submission: July 1, 2009

Submit final study reports to this NDA. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated "**Required Pediatric Assessment**".

POSTMARKETING REQUIREMENTS UNDER 505(o)

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Act of 2007 (FDAAA) amends the FDCA to authorize FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)). This provision took effect on March 25, 2008.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess the signal of a serious risk of nasal septal perforation, which has been associated with the use of an earlier formulation of olopatadine hydrochloride nasal spray containing povidone. Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA has not yet been established and is thus not sufficient to assess this signal of a serious risk. Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess this signal of a serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct a postmarketing clinical trial of Patanase Nasal Spray to assess this signal of a serious risk.

You are required to conduct the following clinical trial:

1. A one-year, controlled clinical trial in patients with perennial allergic rhinitis to assess the long term safety of povidone-free olopatadine hydrochloride nasal spray with respect to nasal septal perforation. We also request that you assess the long term safety of this product with respect to local nasal adverse effects, including epistaxis and nasal ulceration, as well as systemic effects. Include at least the following three treatment

groups: povidone-free olopatadine hydrochloride nasal spray, vehicle placebo with pH matching olopatadine hydrochloride nasal spray, and vehicle placebo with normal pH to evaluate if the low pH of the formulation has an effect on local nasal safety. Submit a labeling supplement reflecting the results of the clinical trial. The timetable you have submitted for this trial states that you will conduct this trial according to the following schedule:

Protocol Submission:	July 2008
Trial Start Date:	November 2008
Final Report Submission:	November 2012

Please submit the protocol to your IND for this product. Submit the final report to this NDA. Please use the following designators to prominently label all submissions, including supplements, relating to this postmarketing requirement as appropriate:

- **Required Postmarketing Trial Protocol under 505(o)**
- **Required Postmarketing Trial Final Report under 505(o)**
- **Required Postmarketing Trial Correspondence under 505(o)**

You are required to report periodically to FDA on the status of any required clinical trial pursuant to sections 505(o)(3)(E)(ii) and 506B of the FDCA, as well as 21 C.F.R. 314.81. Under section 505(o)(3)(E)(ii), you are also required to periodically report to FDA on the status of any study or trial otherwise undertaken to investigate a safety issue associated with Patanase Nasal Spray.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling text for the package insert, patient package insert, and patient instructions for use submitted March 26, 2008. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 21-861."

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on March 26, 2008, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 21-861**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) 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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

METHODS VALIDATION

Please submit one market package of the drug product when it is available.
We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

REPORTING REQUIREMENTS

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 Miranda Raggio, Regulatory Project Manager, at (301) 796-2109.

Sincerely,

{See appended electronic signature page}

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

Attachments: PI Insert
Patient Instructions for Use

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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