DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202129/S-004
NDA 202129/S-005
NDA 202129/S-006

**SUPPLEMENT APPROVAL**

Takeda GmbH
c/o Sunovion Pharmaceuticals, Inc.
84 Waterford Drive
Marlborough, MA 01752

Attention: Sonya Roeloffzen
Associate Director, Regulatory Affairs

Dear Ms. Roeloffzen:

Please refer to your supplemental New Drug Applications (sNDAs) dated December 20, 2013 (S-004), and August 27, 2014 (S-005 and S-006), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zetonna (ciclesonide) Nasal Aerosol.

We acknowledge receipt of your amendments dated January 31, March 17, and 21, August 28, September 26, and October 13, 15, and 20, 2014.

This "Prior Approval" supplemental new drug application proposes changes to the product label to include information regarding four post marketing clinical studies.

## APPROVAL & LABELING

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

## CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

## 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 studies requirement for ages 2 to 5 years because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group **and** is not likely to be used in a substantial number of pediatric patients in this group.

We note that you have fulfilled the pediatric studies requirement for all relevant pediatric age groups for this application.

## FULFILLMENT OF POSTMARKETING REQUIREMENT/COMMITMENTS

Your submission dated December 20, 2013, contained the final report for the following postmarketing requirements listed in the January 20, 2012, approval letter for NDA 202129.

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| 1864-1 | Conduct a 6-week double-blind, placebo-controlled HPA axis trial with ciclesonide nasal aerosol in patients with PAR 6 to 11 years of age (Study 060-308). This trial will evaluate the effect of ciclesonide nasal aerosol (74 mcg) compared to placebo on HPA axis as measured by serum cortisol over 6 weeks of treatment. Additionally the steady-state PK profile after 6 weeks of treatment and the relationship between study drug exposure and change in cortisol exposure will be investigated. |

1864-7 Conduct a randomized clinical trial in adolescent (age 12 years and older) and adult patients with perennial allergic rhinitis of a minimum of 6 months duration to evaluate the long term safety of ciclesonide nasal aerosol as measured by local nasal and ocular assessments. Include the active comparator OMNARIS (ciclesonide) Nasal Spray.

We have reviewed your submission and conclude that the above commitments were fulfilled.

Your submission dated August 27, 2014, contained the final report for the following postmarketing requirements listed in the January 20, 2012, approval letter for NDA 202129.

1864-2 Conduct a 2-week double blind, placebo-controlled, efficacy and safety trial with ciclesonide nasal aerosol in patients with SAR 6 to 11 years of age (Study 060-305). The proposed adolescent and adult dose and at least one lower dose will be studied.

1864-3 Conduct a 12-week double-blind, placebo-controlled, efficacy and safety trial with ciclesonide nasal aerosol in patients with PAR 6 to 11 years of age (Study 060-306). The primary endpoint will be evaluated after 6 weeks of treatment followed by collection of an additional 6 weeks of safety data. The proposed adolescent and adult dose and at least one lower dose will be studied.

We have reviewed your submission and conclude that the above commitments were fulfilled.

**RELEASE FROM POSTMARKETING REQUIREMENTS**

Your submission dated August 27, 2014, reported on the following postmarketing requirements listed in the January 20, 2012, approval letter for NDA 202129.

1864-4 Conduct a 2-week double-blind, placebo-controlled, efficacy and safety trial with ciclesonide nasal aerosol in patients with SAR 2 to 5 years of age.

1864-5 Conduct a 12-week double blind, placebo-controlled, efficacy and safety trial with ciclesonide nasal aerosol in patients with PAR 2 to 5 years of age. The primary efficacy endpoint will be evaluated after 6 weeks of treatment followed by collection of an additional 6 weeks of safety data.

1864-6 Conduct a 6-week double blind, placebo-controlled HPA axis trial with ciclesonide nasal aerosol in patients with PAR 2 to 5 years of age. This trial will evaluate the effect of ciclesonide nasal aerosol compared to placebo on HPA axis as measured by serum cortisol over 6 weeks of treatment. Additionally steady-state PK after 6 weeks of treatment and the

relationship between study drug exposure and change in cortisol exposure will be investigated.

We have reviewed your submission and have determined that you are released from the above requirements as we are waiving the pediatric studies requirement for ages 2 to 5 years because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group **and** is not likely to be used in a substantial number of pediatric patients in this group.

We remind you that there is a postmarketing commitment listed in the January 20, 2012, approval letter that is still open.

## PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

## 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 Colette Jackson, Senior Regulatory Health Project Manager, at (301) 796-1230.

Sincerely,

*{See appended electronic signature page}*

Sally Seymour, M.D.
Deputy Director of Safety
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE: Content of Labeling

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

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/s/

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SALLY M SEYMOUR
10/23/2014