DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022470 **NDA APPROVAL**

Novartis Consumer Health, Inc.
Attention: George Marchesini
Associate Director, Global Regulatory Affairs
200 Kimball Drive
Parsippany, NJ 07054-0622

Dear Mr. Marchesini:

Please refer to your new drug application (NDA) dated January 23, 2009, received January 26, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Nexcede (12.5 mg ketoprofen) oral soluble film.

We acknowledge receipt of your submissions dated January 26, February 19, April 2, May 18, June 16, and 19, August 3, and 25, September 2, and 25, October 9, 16, and 29, and November 11, 17, 18, and 24, 2009.

This new drug application provides for the use of Nexcede (12.5 mg ketoprofen) oral soluble film for the temporary relief of minor aches and pains due to headache, toothache, backache, menstrual cramps, the common cold, muscular aches, minor pain of arthritis, and the temporary relief of fever.

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 agreed-upon labeling text.

LABELING

Submit final printed labeling as soon as they are available, but no more than 30 days after they are printed. The final printed labeling (FPL) must be identical to the enclosed labeling (Nexcede cinnamon and peppermint-flavored pouch labels, and cinnamon-flavored 10- and 20-count carton labels submitted October 29, 2009, and the cinnamon-flavored 40-count, and peppermint-flavored 10-, 20-, and 40-count carton labels submitted November 11, 2009), and must be in the "Drug Facts" format (21 CFR 201.66), where applicable.

The final printed labeling should be submitted 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 Labeling for approved NDA 022470**." Approval of this submission by FDA is not required before the labeling is used.

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 months to less than 6 months for the temporary relief of minor aches and pains due to headache, toothache, backache, menstrual cramps, the common cold, muscular aches, and minor pain of arthritis because necessary studies are impossible or highly impracticable. Assessment and measurement of pain in this population is highly impracticable and some of the labeled conditions do not exist in this population. In addition, we are waiving the pediatric study requirement for ages 0 to less than 6 months for the temporary relief of fever because it is unsafe to treat fever in this population with an over-the-counter medication without consulting a physician.

We are deferring submission of your pediatric studies for ages 6 months to less than 16 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

Deferred pediatric studies under PREA for the treatment of pain in children ages 6 months to less than 16 years:

1575-1

You must conduct a PK trial in children who may benefit from the drug rather than in otherwise healthy pediatric volunteers. You should conduct a single dose PK trial leading into a multiple dose PK trial that would evaluate the safety, tolerability, and pharmacokinetics of an appropriate dose of ketoprofen in children. We recommend recruitment of children in the following age groups, which have been known for differences in developmental physiology as it relates to drug clearance:

- 6 to < 12 months
- 12 to < 24 months
- 2 to < 6 years
- 6 to < 16 years

A minimum of 12 children are required per age group for traditional pharmacokinetic analysis in each of the age groups indicated above. Alternatively, you may consider population PK analysis by the sparse sampling approach. Ensure that the distribution of pediatric patients across gender, age, and weight ranges is reasonably even. The number of children should be based on being able to estimate, for each age group, the mean apparent CL and apparent volume of distribution, with a standard error of 20% or less. The trial(s) may be conducted in a sequential fashion such that older children are exposed to the test product before younger children.

Final Study Report Submission: November 2010

1575-2

You must provide efficacy data for children less than 16 years of age for the pain indication. You must conduct adequate and well-controlled superiority trials demonstrating efficacy for children ages 6 months to less than 16 years. These trials should be conducted using a pain model or models suitable for an over-the-counter population.

Final Study Report Submitted: October 2012

1575-3

You must conduct a safety trial on a sizable population of children ages 6 months to less than 16 years. This trial must include adequate representation of the age groups and be conducted in a symptomatic population under "actual use" conditions.

Final Study Report Submission: June 2014

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(s)**".

This product is appropriately labeled for use in children ages 16 to less than 17 years for these indications. Therefore, no additional studies are needed in this pediatric group.

POSTMARKETING COMMITMENTS SUBJECT TO THE REPORTING REQUIREMENTS OF SECTION 506B

We acknowledge your written commitment to conduct the following postmarketing study as described in your submission dated November 24, 2009, and as outlined below:

1575-4

Conduct a randomized, placebo-controlled study to assess the CPK in users of the ketoprofen oral soluble film. The study will enroll healthy subjects. Subjects will be excluded if they are at risk for CPK elevations for reasons other than the study drug. CPKs will be assessed at baseline and at the end of the study. Participants will take the study medication for ten days, the duration of use allowed on the product label. Normal physical activity will be allowed but physical exercise will be restricted. All

subjects will be queried as to exercise and other exposures that could raise CPK during the course of the study. All CPK elevations will be followed to resolution and adverse events will be recorded. The study will enroll 200 subjects in the ketoprofen arm and 100 in the placebo arm.

Final Protocol Submission: by June 2010
Study Completion Date: by March 2011
Final Report Submission: by December 2011

PROMOTIONAL MATERIALS

Please submit two market packages of the drug product when it is available.

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
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

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 Neel Patel, Regulatory Project Manager, at (301) 796-0970.

Sincerely,

{See appended electronic signature page}

Andrea Leonard-Segal, M.D.
Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

Enclosure: Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22470	ORIG-1	NOVARTIS CONSUMER HEALTH INC	KETOPROFEN ORAL-ORAL DISSOLVING STRIPS

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

/s/

ANDREA LEONARD SEGAL
11/25/2009