DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-159 **NDA APPROVAL**

Novalar Pharmaceuticals, Inc.
12555 High Bluff Drive, Suite 300
San Diego, CA 92130

Attention: Laura A. Navalta
Vice President of Clinical Operations

Dear Ms. Navalta:

Please refer to your new drug application (NDA) dated April 9, 2007, received April 9, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OraVerse (phentolamine mesylate) Injection 0.4 mg (0.235 mg/mL).

We acknowledge receipt of your submissions dated June 8 and 22, August 6, October 19, November 9, 14, and 16, December 11 and 20 (4), 2007, and January 23, 2008.

This new drug application provides for the use of OraVerse (phentolamine mesylate) Injection for the reversal of soft-tissue anesthesia, i.e., anesthesia of the lip and tongue, and the associated functional deficits resulting from an intraoral submucosal injection of a local anesthetic containing a vasoconstrictor.

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.

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. 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 22-159."

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels and/or submitted carton and immediate container labels 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 22-159**." 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 may render the product misbranded and an unapproved new drug.

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 pediatric patients less than 2 years of age because the necessary studies are impossible or highly impracticable. This is because the number of patients in this age range who present for dental procedures requiring the use of a local anesthetic with a vasoconstrictor is too small to allow an appropriate study to be conducted.

We are deferring submission of your pediatric study for pediatric patients 2 to 6 years of age for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81(FOR NDAs)/21 CFR 601.70(FOR BLAs) and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

1. Assessment of efficacy and safety of OraVerse in patients from 2-6 years of age. This study should be a randomized, sham-injection controlled, double-blinded study comparing the times to return of normal sensation and normal function following the injection OraVerse or a sham injection administered to patients undergoing dental procedures requiring the administration of a local anesthetic agent combined with a vasoconstrictor. Specifically, the following clinical endpoints should be assessed using validated metrics:

    a. Time to return of normal sensation of the lip and, where applicable, the tongue

b. Time to return of normal function for speech, smiling, drinking, eating and not drooling

Safety assessments should include heart rate, blood pressure, oral cavity examinations, assessments for nerve injury, and adverse events.

The study should include a minimum of 100 subjects uniformly distributed by age and evenly distributed by treatment within 1-year age groups.

Final Report Submission: May 2011

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

This product is appropriately labeled for use in pediatric patients 6 years of age and above for this indication. Therefore, we note that you have fulfilled the pediatric study requirement for ages 6 to 17 years for this application and no additional studies are needed in this pediatric group.

Submit clinical and nonclinical protocols to your IND for this product. Submit 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 Requirement Protocol**", "**Postmarketing Study Requirement Final Report**", or "**Postmarketing Study Requirement Correspondence**."

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 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.

Please submit one market package 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
Suite 12B05
5600 Fishers Lane
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 Dominic Chiapperino, Regulatory Project Manager, at (301) 796-1183.

Sincerely,

{See appended electronic signature page}

Rigoberto Roca, M.D.
Deputy Director
Division of Anesthesia, Analgesia, and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: package insert, carton and container labeling, blister backing, and cartridge 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.

/s/

Rigoberto Roca

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