DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 16968/S-029

SUPPLEMENT APPROVAL

Alcon Laboratories, Inc.
Attention: Suzanne Cadden, MSc
Head of Regulatory Affairs, USA
6201 South Freeway, Mail Code TA6-8
Fort Worth, TX 76134

Dear Ms. Cadden:

Please refer to your Supplemental New Drug Application (sNDA) dated July 27, 2015, received July 28, 2015, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Miostat (carbachol intraocular solution, USP) 0.01%. We also refer to your amendment dated September 4, 2015.

This "Prior Approval" supplemental new drug application provides for the following revisions to the package insert (additions are underlined).

In the section titled, **WARNINGS,** a new sentence is added as follows:

WARNINGS
For single-dose intraocular use only. Discard unused portion. Intraocular carbachol 0.01% should be used with caution in patients with acute cardiac failure, bronchial asthma, peptic ulcer, hyperthyroidism, G.I. spasm, urinary tract obstruction and Parkinson's disease.
The vial stopper contains natural rubber (latex) which may cause severe allergic reactions.

In the section titled, **ADVERSE REACTIONS,** new sentences are added as follows:

ADVERSE REACTIONS
Ocular: Corneal clouding, persistent bullous keratopathy, retinal detachment and postoperative iritis following cataract extraction have been reported.
Systemic: Side effects such as flushing, sweating, epigastric distress, abdominal cramps, tightness in urinary bladder, and headache have been reported with topical or systemic application of carbachol.
The following additional reactions have been identified during post-approval use of MIOSTAT (carbachol intraocular solution, USP) in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to MIOSTAT, or a combination of these factors, include: corneal edema, drug

effect prolonged (miosis), eye inflammation, eye pain, intraocular pressure increased, ocular hyperemia, vision blurred, visual impairment, and vomiting.

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 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).

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 Lois Almoza, M.S., Regulatory Health Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Deputy Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE:
Package Insert

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

/s/

WILEY A CHAMBERS
01/21/2016