DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22369/S-008
NDA 22369/S-010

SUPPLEMENT APPROVAL

Allergan, Inc.
Attention: Sally K. Wixson
Manager, U.S. Regulatory Affairs
2525 Dupont Drive
P. O. Box 19534
Irvine, CA 92623-9534

Dear Dr. Wixson:

Please refer to your Supplemental New Drug Applications (sNDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for LATISSE (bimatoprost ophthalmic solution), 0.03% as follows:

S-008, dated and received March 7, 2013, which provides for revisions to sections 5.8 Use with Contact Lenses, 6.1 Clinical Studies Experience, 6.2 Postmarketing Experience, 16 How Supplied/ Storage and Handling and 17.8 /Patient Counseling /Use with Contact Lenses of the Package Insert and

S-010, received March 4, 2014, which provides for the revision of the 8.4 Pediatric Use section to the Package Insert.

We also acknowledge your amendments to S-008 dated March 4, and September 3, 2014. Your submission dated March 4, 2014, constituted a complete response to our Complete Response letter dated February 11, 2014. We further acknowledge your amendments to S-010 dated April 1, April 14, September 2, and September 3, 2014.

Supplement S-008 provides for revisions to the Package Insert as follows (deletions are in ~~strikethrough~~ and additions are underlined):

1. The first sentence of the 5.8 Use with Contact Lenses section is revised as follows:

   LATISSE® contains benzalkonium chloride, which may be absorbed by and cause discoloration of soft contact lenses.

2. The second paragraph in the 6.1 Clinical Studies Experience section is revised as follows:

The most frequently reported adverse ~~events~~ reactions were eye pruritus, conjunctival hyperemia, skin hyperpigmentation, ocular irritation, dry eye symptoms, and periorbital erythema ~~of the eyelid~~. These ~~events~~ reactions occurred in less than 4% of patients.

3. The third sentence in the 6.2 Postmarketing Experience section, is revised as follows:

   The following reactions have been identified during postmarketing use of **LATISSE®** 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 **LATISSE®**, or a combination of these factors, include: eye swelling, eyelid edema, hypersensitivity (local allergic reactions), lacrimation increased, madarosis and trichorrhexis (temporary loss of a few lashes to loss of sections of eyelashes, and temporary eyelash breakage, respectively), periorbital and lid changes associated with a deepening of the eyelid sulcus, rash (including macular, erythematous), skin discoloration (periorbital), and vision blurred.

4. The statement in 16 How Supplied / Storage and Handling is revised as follows:

   Storage: ~~**LATISSE®** should be stored~~ Store at 2-25 ºC (36-77 ºF).

5. The 17.8 Use with Contact Lenses section of the Patient Counseling Information is revised as follows:

   ~~Patients should be advised~~ Advise patients that **LATISSE®** solution contains benzalkonium chloride, which may be absorbed by and cause discoloration of soft contact lenses. Contact lenses should be removed prior to application of **LATISSE®** and may be reinserted 15 minutes following its administration.

Supplement S-010 provides for revisions to section8.4 Pediatric Use as follows:

8.4 Pediatric Use

~~Safety and effectiveness in pediatric patients have not been established.~~

Use of **LATISSE®** was evaluated in a sixteen week double-masked, randomized, vehicle-controlled study conducted in pediatric patients who were post-chemotherapy or had alopecia areata, and adolescents who had hypotrichosis with no associated medical condition. No new safety issues were observed. The results of the Global Eyelash Assessment are provided in Table 1.

Table 1. Number (%) of subjects with at least a 1-grade increase from baseline at month 4 in Global Eyelash Assessment

	Age Range (years)	**LATISSE®**	Vehicle	Difference (95% CI)
Adolescents with hypotrichosis (N=40)	15 - 17	19/26 (73%)	1/14 (7%)	66% (44%, 88%)
Post Chemotherapy Pediatric Patients (N=16)	5 - 17	11/13 (85%)	3/3 (100%)	-15% (-35%, 4%)
Alopecia Areata Pediatric Patients (N=15)	5 - 17	4/9 (44%)	2/6 (33%)	11% (-39%, 61%)

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text which is identical to the labeling submitted on September 3, 2014.

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 study(ies) requirements for ages less than 5 years old because the necessary studies are impossible or highly impracticable. This product is appropriately labeled for use in pediatric population ages ≥ 5 to 17 years. Therefore, no additional pediatric studies are needed at this time.

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 Michael Puglisi, Regulatory Project Manager, at (301)-796-0791.

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: Content of Labeling

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
09/04/2014