CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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STATISTICAL REVIEW(S)

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Translational Sciences
Office of Biostatistics

STATISTICAL REVIEW AND EVALUATION

CLINICAL STUDIES

NDA/BLA #:	NDA 206276
Supplement #:	0000
Drug Name:	Olopatadine Hydrochloride Ophthalmic Solution 0.77%
Indication(s):	Treatment of Itching Associated with Allergic Conjunctivitis
Applicant:	Alcon
Date(s):	Submitted: 07/30/2014 PDUFA date: 01/30/2015
Review Priority:	Priority
Biometrics Division:	DBIV
Statistical Reviewer:	Yunfan Deng, Ph.D.
Concurring Reviewers:	Yan Wang, Ph.D.
Medical Division:	Division of Transplant and Ophthalmology Products
Clinical Team:	Wiley Chambers, MD, Deputy Division Director William Boyd, MD, Team Leader
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Keywords: itching, redness, allergic conjunctivitis, superiority

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1 EXECUTIVE SUMMARY

The applicant (Alcon) seeks approval of Olopatadine Hydrochloride Ophthalmic Solution, 0.77% (Olopatadine HCl Solution, 0.77%, also referred to as Olopatadine 0.77% throughout this review) for the treatment of ocular itching associated with allergic conjunctivitis. In 1996, Olopatadine HCl Solution 0.1% (PATANOL®) was approved for **twice daily** dosing in the U.S for the treatment of the signs and symptoms of allergic conjunctivitis. A higher concentration formulation, Olopatadine HCl Solution 0.2% (PATADAY®) was also approved for dosing **once per day** in the U.S. for the treatment of ocular itching (**but not redness**) associated with allergic conjunctivitis since 2004. This submission is for a new formulation of olopatadine having a 0.77% concentration of the active ingredient, olopatadine hydrochloride for dosing **once daily**. By increasing the concentration of olopatadine hydrochloride to 0.77%, the applicant intended to demonstrate that the new formulation would extend the benefit offered by Olopatadine, 0.2% (PATADAY®) while maintaining its safety. In order to support the approval of this new formulation, the applicant submitted two pivotal efficacy studies: Study C-10-126, and Study C-12-053.

Studies C-10-126 and C-12-053 were similarly designed phase 3 studies. Both were multicenter, randomized, double-masked, active and vehicle controlled, parallel-group studies and used the conjunctival allergen challenge (CAC) model to evaluate the safety and efficacy of Olopatadine 0.77% versus Vehicle or active comparators in the treatment of ocular itching associated with allergic conjunctivitis. Both studies were conducted in patients at least 18 years of age with a history of seasonal and/or perennial allergic conjunctivitis for at least 1 year prior to study entry and a positive allergic skin test within 24 months prior to study entry. Study C-10-126 had PATADAY and Vehicle as comparators. Study C-12-053 had PATADAY, PATANOL and Vehicle as comparators; however, PATANOL was dosed only once (instead of the approved twice-a-day regimen) at Visit 3A (the day before the 24-hour duration-of-action efficacy evaluation) and Visit 4.

The primary efficacy variable for both studies was patient-evaluated ocular itching severity scores (assessed using a 0-4 scale with 0.5 unit increments: 0 = none, 4 = incapacitating itch). In Study C-10-126, the primary efficacy endpoints were patient-evaluated ocular itching at 3, 5, and 7 minutes post-CAC at both Visits 4B (16-hour duration-of-action) and 5 (onset-of-action). In Study C-12-053, the primary efficacy endpoints were patient-evaluated ocular itching at 3, 5, and 7 minutes post-CAC at both Visit 3B (24-hour duration-of-action) and Visit 4 (onset-of-action).

The primary efficacy objectives for Study C-10-126 were to demonstrate the superiority of Olopatadine 0.77% compared to Vehicle for the treatment of ocular itching associated with allergic conjunctivitis at:

- Onset-of-action
- 16-hour duration-of-action

A secondary efficacy objective in this study was to [redacted] (b) (4)

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