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STATISTICAL REVIEW(S)



U.S. Department of Health and Human Services
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STATISTICAL REVIEW AND EVALUATION

CLINICAL STUDIES

NDA/BLA #: NDA 206276
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Applicant: Alcon
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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

(b) (4)

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