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STATISTICAL REVIEW(S)

U.S. Department of Health and Human Services
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Office of Translational Sciences
Office of Biostatistics

STATISTICAL REVIEW AND EVALUATION

CLINICAL STUDIES

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1. EXECUTIVE SUMMARY

1.1 Conclusions and Recommendations

In this submission, the Applicant seeks approval of preservative-free (PF) tafluprost 0.0015% ophthalmic solution administered once daily for the treatment of elevated intraocular pressure (IOP). The Applicant submitted three non-inferiority efficacy studies (two timolol non-inferiority studies [15-003 and 001] and one Latanoprost Non-Inferiority Study [74458]), and a study comparing the PC formulation and PF formulation (Study 77550).

For study 15-003 comparing preservative-containing (PC) tafluprost with PC timolol, both PC tafluprost and the active comparator PC timolol showed IOP-lowering effect throughout the 12-month study period. Tafluprost reached the predetermined criteria for non-inferiority (1.5 mmHg) at each visit and time point using timolol as the active comparator.

For study 001 comparing PF tafluprost versus PF timolol, both PF tafluprost and the active comparator (PF timolol) showed IOP-lowering effect throughout the 12 weeks of treatment. The IOP-lowering effect of PF tafluprost was within the 1.5 mmHg non-inferiority margin compared to PF timolol at all visits and time points.

Study 77550 investigated the pharmacodynamics (as expressed in IOP) of the preserved and unpreserved formulation of tafluprost 0.0015% eye drops in patients with open-angle glaucoma or ocular hypertension. For both the preservative-containing and preserve-free formulation, a similar and clear IOP-lowering effect was seen already at week 1 and the IOP-lowering effect was sustained and similar for both formulations at week 4.

For study 74458, both PC tafluprost and PC latanoprost reduced IOP throughout the 24 months treatment period. However, tafluprost did not reach the predetermined criterion for non-inferiority (1.5 mmHg) versus latanoprost.

Using the non-inferiority margin of 1.5 mmHg, both studies 15-003 and 001 demonstrated non-inferiority of tafluprost 0.0015% to timolol 0.5% in reducing elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension in both preservative-containing and preservative-free formulation. Study 77550 demonstrated that the IOP lowering effects for the PC formulation and the PF formulation were similar.

Based on the totality of the evidence provided by these pivotal studies, we recommend the approval of PF tafluprost 0.0015% dosed once daily for the treatment of elevated intraocular pressure in patients with open glaucoma or ocular hypertension.

1.2 Brief Overview of Clinical Studies

The Phase III program consisted of three pivotal non-inferiority efficacy studies (two timolol non-inferiority studies [15-003 and 001] and one Latanoprost Non-Inferiority Study [74458]), an adjunctive therapy to timolol study (74460) examining the additive effect of tafluprost to timolol,

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