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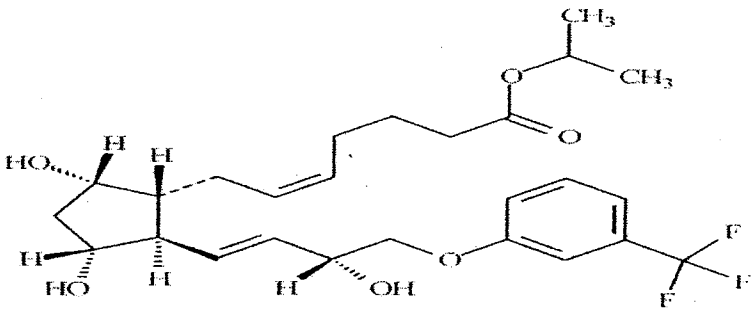
APPLICATION NUMBER:

21-994

MEDICAL REVIEW

CLINICAL REVIEW

Application Type	NDA 21-994
Submission Number	000
Submission Code	Original
Letter Date	11/18/05
Stamp Date	11/21/05
PDUFA Goal Date	09/21/06
Reviewer Name	Martin P. Nevitt, M.D., M.P.H.
Review Completion Date	5/09/06
Established Name	travoprost ophthalmic solution 0.004%
(Proposed) Trade Name	Travatan Z
Therapeutic Class	Prostaglandin $F_{2\alpha}$ analogue
Applicant	Alcon Research, Ltd. 6201 South Freeway P.O. Box 19534 Fort Worth, TX 76134-2099 817-551-4933 Angela C. Kothe, OD, PhD Associate Director, Regulatory Affairs
Priority Designation	S
Structure	$C_{26}H_{35}F_3O_6$



Dosing Regimen	One drop in the affected eye(s) once-daily in the evening
Indication	Reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension who are intolerant of intraocular lowering medications or are insufficiently responsive (failed to achieve target IOP determined after multiple measurements over time) to another intraocular pressure lowering medication
Intended Population	Patients 18 years or older with open angle glaucoma or ocular hypertension

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1 EXECUTIVE SUMMARY

1.1 Recommendation on Regulatory Action

From a clinical perspective, NDA 21–994 is recommended for approval for the treatment of elevated intraocular pressure (IOP) in patients with open angle glaucoma or ocular hypertension who are intolerant of intraocular lowering medications or insufficiently responsive (failed to achieve target IOP determined after multiple measurements over time) to another intraocular pressure lowering medication.

The submitted bioequivalence trial (study C-04-17) supports approval of Travatan Z, aka Travatan BAC-free. Travatan Z was developed for those patients who may be intolerant of the preservative benzalkonium chloride.

Study C-04-17 was a multicenter, phase 3 safety and efficacy trial. This safety/efficacy study was designed to demonstrate bioequivalence of Travatan Z (the BAC-free formulation of travoprost ophthalmic solution, 0.004%) to the marketed formulation of travoprost ophthalmic solution, 0.004% (Travatan), with both dosed once-daily in the evening in patients with open-angle glaucoma or ocular hypertension.

The primary efficacy endpoint, mean intraocular pressure, is demonstrated to be equivalent when comparing travoprost ophthalmic solution, 0.004% (Travatan Z), to the previously approved drug, travoprost ophthalmic solution, 0.004% (Travatan). Equivalence is defined as the two sided 95% confidence interval being less than 1.5 mmHg at each direct group comparison over multiple times over a three month period and being less than 1.0 mmHg for the majority of direct group comparisons. Travatan (NDA 21-257) was first approved in March 2001 for the reduction of elevated IOP in patients with open-angle glaucoma or ocular hypertension who are intolerant of intraocular lowering medications or are insufficiently responsive (failed to achieve target IOP determined after multiple measurements over time) to another intraocular pressure lowering medication.

The recommended dosing regimen is one drop in the affected eye(s) once daily in the evening.

1.2 Recommendation on Postmarketing Actions

1.2.1 Risk Management Activity

No additional clinical trials or postmarketing surveillance studies are required.

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