

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-463 / S-026

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW # 1	1. ORGANIZATION HFD-550	2. NDA Number(s) 19-463
3. Name and Address of Applicant (City & State): Merck & Co., Inc. Sumneytown Pike, P.O. Box 4, BLA-20 West Point, PA 19486 (Virginia G Snyder at telephone 484-344-7984)		4. AF No.
		5. Supplement(s) Number(s) Date(s) SLR026 27-June-2003
6. Drug Name: TIMOPTIC™ in OCUDOSE™	7. Nonproprietary Name: Timolol Maleate	8. Amendments & Other (reports, etc.) - Dates
9. Supplement Provides For: the addition of pH and osmolarity to the label in the DESCRIPTION section. (CBE-0)		Annual Report
10. Pharmacological Category: β ₁ and β ₂ adrenergic receptor blocking agent used to reduce intraocular pressure	11. How Dispensed: <input checked="" type="checkbox"/> Rx <input type="checkbox"/> OTC	12. Related IND(s)/ NDA(s)/DMF(s) NDA 19-463/SLR022
13. Dosage Form(s): Solution	Potency(ies): 0.25%, 0.5%	
15. Chemical Name and Structure: (-)-1-tert-butylamino-3-[(4-morpholino-1,2,5-thiadiazol-3-y)oxy]-2-prpanol maleate (1:1) salt		16. Records/Reports Current: <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No Reviewed: <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
17. Comments: The pH and osmolarity is added to the label in the DESCRIPTION section. However, the location of the additional sentence was suggested to changed for the purpose of smooth reading		
18. Conclusions and Recommendations: The proposed labeling is acceptable. From CMC viewpoint this supplement is recommended for approval.		
CC: Original NDA 19-463 HFD-550/Division File HFD-550/Med/Wchambers HFD-550/LNg HFD-550/CSO/MPuglisi HFD-830/CwChen HFD-550/YLu R/D initialed by : Linda Ng		
19. REVIEWER		
Name: Yong-de Lu Ph.D.	Signature:	Date Completed: 03-Dec-2003

REVIEW NOTES

Firm submitted: (The additional sentence is noted by bold font.)

DESCRIPTION

Preservative-free Ophthalmic Solution TIMOPTIC is supplied in OCUDOSE*, a unit dose container, as a sterile, isotonic, buffered, aqueous solution of timolol maleate in two dosage strengths: Each mL of Preservative-free TIMOPTIC in OCUDOSE 0.25% contains 2.5 mg of timolol (3.4 mg of timolol maleate). **The pH of the solution is approximately 7.0, and the osmolarity is 252-328 mOsm.** Each mL of Preservative-free TIMOPTIC in OCUDOSE 0.5% contains 5 mg of timolol (6.8 mg of timolol maleate). Inactive ingredients: monobasic and dibasic sodium phosphate, sodium hydroxide to adjust pH, and water for injection.

Reviewer recommended:

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this page is the manifestation of the electronic signature.**

/s/

Yong-De Lu
12/3/03 11:22:09 AM
CHEMIST

Linda Ng
12/3/03 01:09:25 PM
CHEMIST
PM to prepare AP letter