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APPLICATION NUMBER: NDA 19777/S26

CHEMISTRY REVIEW(S)

JUL 11 1995

CHEMIST'S REVIEW		1. ORGANIZATION HFD-110	2. NDA Number 19-777
3. Name and Address of Applicant (City & State) Zeneca Pharmaceuticals Wilmington, DE 19897		4. Supplement(s) Number(s) Date(s) S-026 6 Jun 95	
5. Drug Name Zestril	6. Nonproprietary Name Lisinopril	7. Amendments & Other (reports, etc) - Dates	
8. Supplement Provides For: A change in solvent used in the manufacture of lisinopril TFA ester from 1,1,1-trichloroethane to t-butyl methyl ether/methylcyclohexane.			
9. Pharmacological Category Antihypertensive	10. How Dispensed <input checked="" type="checkbox"/> Rx <input type="checkbox"/> OTC	11. Related IND(s)/NDA(s)/DMF(s) NDA 19-558 Prinivil, Merck	
12. Dosage Form(s) TCM	13. Potency(ies) 2.5, 5, 10, 20, 40-mg		
14. Chemical Name and Structure		15. Records/Reports Current <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No Reviewed <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
16. Comments: The purpose of the proposed change, described in Attachment I, in the manufacturing procedure for lisinopril TFA ester, the precursor of lisinopril, is to discontinue the use of 1,1,1-trichloroethane as a solvent in compliance with the requirements of the Montreal protocol. The manufacturer proposes to substitute a mixture of t-butyl methyl ether and methylcyclohexane. Attachment II provides revised specifications for the ester. The only change is in the specifications for the residual solvents. The specification for _____ has been deleted. Specifications for t-butyl methyl ether and methylcyclohexane are NMT 1% of each, with the total not to exceed 1%. No changes have been made in the specifications for lisinopril.			
17. Conclusions and Recommendations: APPROVAL is recommended.			
18.		REVIEWER/ <i>[Signature]</i>	Date Completed 5 Jul 95
Name James H. Short			
Distribution: <input type="checkbox"/> Original Jacket <input type="checkbox"/> Reviewer <input type="checkbox"/> Division File <input type="checkbox"/> CSO <input type="checkbox"/> District			

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R/D Init: RWalters/

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