

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER: NDA 19787/S008**

**CORRESPONDENCE**



Inna Kissen, PhD  
Associate Director—Drug Regulatory Affairs

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Raymond Lipicky, M.D., Director  
Division of Cardio-Renal  
Drug Products (HFD-110)  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852

NDA NO. 19-787 REF. NO. S-008

NDA SUPPL. FOR. SCS



RE: Norvasc (amlodipine besylate) Tablets  
NDA #19-787

Dear Dr. Lipicky:

Please find attached a supplemental application for Norvasc (amlodipine besylate) Tablets, NDA #19-787 that requests the approval of a change in the tablet specification. It is proposed that the specification for the UK-55,410 content in Norvasc Tablets be changed form "not greater than %" to "not greater than %".

is a major metabolite in man, dogs and rats. It is observed as a process related substance in amlodipine besylate drug substance and drug product. Oxidation of amlodipine to this pyridine derivative represents the major matabloic pathway in man. The requested specification change is not significant either in terms of clinical effect or safety as demonstrated in the literature.

The enclosed supplemental submission contains:

- Appendix I: Diagram of Amlodipine Metabolic Pathway
- Appendix II: Response to FDA's Comments submitted April 6, 1992
- Appendix III: Standard Test Procedures
- Appendix IV: Metabolism and Kinetics of Amlodipine in Man
- Appendix V: Proposed and Currently Approved Specification-R's for Norvasc Tablets 2.5, 5, and 10mg.

ORIGINAL

A field copy of this supplemental application is submitted to the Brooklyn District Office.

Please review the enclosed supplemental application.

If you have any questions, please call my office at (212) 573-2503.

Sincerely,



Inna Kissen, Ph.D.

IK:amw

ENCLOSURE

norvasc2/7

CONFIDENTIAL/TRADE SECRET INFORMATION  
SUBJECT TO 18-USE-1905 AND TO WHICH ALL  
CLAIMS OF PRIVILEGE AND CONFIDENTIALITY  
ARE ASSERTED IN BOTH STATUTORY AND  
COMMON LAW.