

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER: NDA 19787/S010**

**CORRESPONDENCE**

ORIGINAL

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NDA NO. 19-787 REF. NO. S-910

NDA SUPPL FOR SES SCM

January 2, 1996

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 Evaluation  
1451 Rockville Pike  
Rockville, Maryland 20852

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



Dear Dr. Lipicky:

Please find attached a supplemental application for Norvasc Tablets (amlodipine besylate), NDA #19-787 that requests approval for an alternate method to purify amlodipine besylate in the event of excess ammonium besylate.

The currently approved process to manufacture amlodipine besylate drug substance includes two purification methods for amlodipine besylate. One is

approval of a . This supplement requests  
method for amlodipine besylate. as an alternate purification  
option is used, it is followed by the currently approved method. The use of the  
has been demonstrated to effectively remove excess  
in amlodipine besylate drug substance.

Analytical data for amlodipine besylate drug substance  
manufactured using the proposed followed by  
method show that the quality is comparable to  
drug substance manufactured according to the currently  
approved process. There is no change in the impurity profile  
to the finished drug substance as a result of this process  
change, and the chemistry, synthetic route, and finished  
drug substance specifications are unchanged.

This supplement contains the currently approved process  
description for amlodipine besylate, }

(appendix I), and the proposed process description, (appendix II) which incorporates the use of the alternate purification method. Analytical data for two commercial scale lots of amlodipine besylate manufactured using purification method are provided in appendix III, along with analytical data for one lot of amlodipine besylate manufactured according to the currently approved process. The currently approved finished drug substance specification for amlodipine besylate is also provided for reference (appendix IV).

One lot of amlodipine besylate drug substance manufactured using the proposed alternate purification method has been placed into the drug substance stability program.

Please review the attached supplement.

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

Sincerely,



Inna Kissen, Ph.D.

IK:amw  
Enclosure  
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