DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020528 S-0012 **SUPPLEMENT APPROVAL**

Abbott Laboratories
Attention: Richard Leber
Manager
Abbott Laboratories (GPRA)
Dept. PA76/ Bldg. AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Mr. Leber:

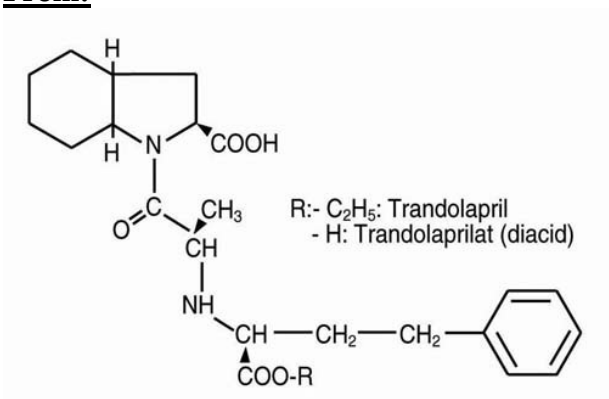
Please refer to your December 11, 2006 Supplemental New Drug Application (sNDA), received December 12, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Mavik (trandolapril) 1, 2 and 4 mg Tablets.

We acknowledge receipt of your submission dated October 26, 2009 and received October 27, 2009. Your submission of October 26, 2009 constituted a complete response to our August 3, 2009 action letter.

This Prior Approval supplemental new drug application provides for the following labeling changes:

1. Under the **DESCRIPTION** section, the chemical description and structural formula have been revised:

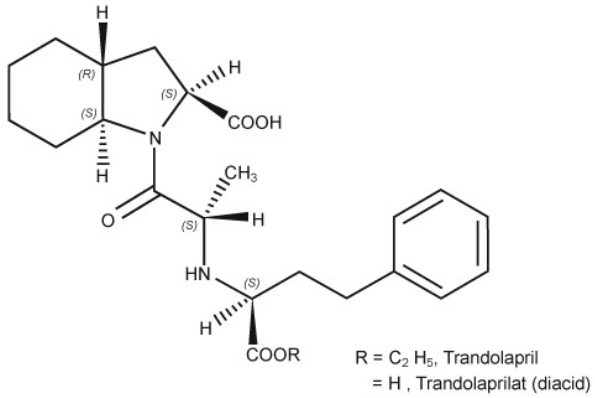
   From:



   M.W. = 430.54
   Melting Point = 125°C

Trandolapril is a colorless, crystalline substance that is soluble (> 100mg/mL) in chloroform, dichloromethane, and methanol. MAVIK tablets contain 1 mg, 2 mg, or 4 mg of trandolapril for oral administration. Each tablet also contains corn starch, croscarmellose sodium, hypromellose, iron oxide, lactose, povidone, sodium stearyl fumarate.

To:



Trandolapril/ -H: Trandolaprilat (diacid)
M.W. = 430.54
Melting Point = 125°C

Trandolapril is a **white or almost white powder** that is soluble (> 100mg/mL) in chloroform, dichloromethane, and methanol. MAVIK tablets contain 1 mg, 2 mg, or 4 mg of trandolapril for oral administration. Each tablet also contains corn starch, croscarmellose sodium, hypromellose, iron oxide, lactose **monohydrate**, povidone, sodium stearyl fumarate.

2. Under the **CLINICAL PHARMACOLOGY, Pharmacokinetics** subsection the half-life description has been modified:

From:

The elimination half lives of trandolapril and trandolaprilat are about 6 and 10 hours, respectively, but, like all ACE inhibitors, trandolaprilat also has a prolonged terminal elimination phase, involving a small fraction of administered drug, probably representing binding to plasma and tissue ACE.

To:

The elimination half life of trandolapril is about 6 hours. At steady state, the effective half-life of trandolaprilat is 22.5 hours. Like all ACE inhibitors, trandolaprilat also has a

prolonged terminal elimination phase, involving a small fraction of administered drug, probably representing binding to plasma and tissue ACE.

3. Under **DRUG INTERACTIONS, Other** subsection, the following language has been modified:

From:

No clinically significant interaction has been found between trandolaprilat and food, cimetidine, digoxin, or furosemide. The anticoagulant effect of warfarin was not significantly changed by trandolapril.

(b) (4)

To:

No clinically significant pharmacokinetic interaction has been found between trandolaprilat and food, cimetidine, digoxin, or furosemide.

The anticoagulant effect of warfarin was not significantly changed by trandolapril.

As with all other inhibitors of RAS, NSAIDs may reduce the antihypertensive effects of trandolapril. Blood pressure monitoring should be increased when any NSAID is added or discontinued in a patient treated with trandolapril.

The hypotensive effect of certain inhalation anesthetics may be enhanced by ACE inhibitors including trandolapril (See **PRECAUTIONS - Surgery/Anesthesia**.)

4. Under **ADVERSE REACTIONS**, the first sentence has been changed:

From:

The safety experience in U.S. placebo-controlled trials included 1067 hypertensive patients, of whom 831 received MAVIK.

To:

The safety experience in U.S. placebo-controlled trials included 1069 hypertensive patients, of whom 832 received MAVIK.

5. Under **ADVERSE REACTIONS**, clinical events were added and deleted with editorial line change modifications:

From:

General Body Function: chest pain.
Cardiovascular: AV first degree block, bradycardia, edema, flushing, hypotension, palpitations.
Central Nervous System: drowsiness, insomnia, paresthesia, vertigo.
Dermatologic: pruritus, rash, pemphigus.
Eye, Ear, Nose, Throat: epistaxis, throat inflammation, upper respiratory tract infection.
Emotional, Mental, Sexual States: anxiety, impotence, decreased libido.
Gastrointestinal: abdominal distention, abdominal pain/cramps, constipation, dyspepsia, diarrhea, vomiting, *pancreatitis*.
Hemopoietic: *decreased leukocytes, decreased neutrophils.*
Metabolism and Endocrine: *increased creatinine, increased potassium,* increased SGPT (ALT).
Musculoskeletal System: extremity pain, muscle cramps, gout.
Pulmonary: dyspnea.

To:

General Body Function
Chest pain, malaise, fever.
Cardiovascular
AV first degree block, bradycardia, edema, flushing, hypotension, palpitations.
Central Nervous System
Drowsiness, insomnia, paresthesia, vertigo.
Dermatologic
Pruritus, rash, pemphigus, alopecia, sweating.
Eye, Ear, Nose, Throat
Epistaxis, throat inflammation, upper respiratory tract infection.
Emotional, Mental, Sexual States
Anxiety, impotence, decreased libido.
Gastrointestinal
Abdominal distention, abdominal pain/cramps, constipation, dyspepsia, diarrhea, vomiting, nausea, dry mouth, pancreatitis.
Hemopoietic
Agranulocytosis, decreased leukocytes, decreased neutrophils.
Metabolism and Endocrine
Increased creatinine, increased potassium, increased liver enzymes including SGPT (ALT) and increased SGOT (AST).
Musculoskeletal System
Extremity pain, muscle cramps, gout.
Pulmonary
Dyspnea, bronchitis

6. Under **DOSAGE AND ADMINISTRATION**, the tablet colors have been capitalized.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed upon labeling text, which is

identical to the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format submitted on October 26, 2009.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call Michael Monteleone, Regulatory Project Manager, at (301) 796-1952.

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm.D.
Deputy Director for Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure:
Content of Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20528	SUPPL-12	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	MAVIK (TRANDOLAPRIL) TABS 1MG/2MG/4MG

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MARY R SOUTHWORTH
04/20/2010