

Meeting Challenges to Profitability

Chapter FastFACTS

- 1. It's particularly important in tough economic times for primary care practices to implement improvements that lead to better quality and efficiency.**
- 2. Physicians who don't budget and forecast in any formal way should learn—or relearn—business basics.**
- 3. Being proactive by having a well-thought-out plan is best to deal with today's financial challenges.**
- 4. Practices need a technology plan that includes a timeline for conversion to new technologies.**
- 5. Smaller practices can survive if they are open to new ways of practicing and doing business.**

It isn't easy to run a profitable primary care practice. Of all the specialties, primary care seems to suffer most from working under a fee-for-service, volume-based payment system amid annual threats of Medicare reimbursement cuts. Those challenges have only increased given today's lackluster U.S. economy. While healthcare reform may have a positive impact on primary care physicians' finances, much of the plan—still under debate—has yet to take effect.

Nonetheless, experts who spoke with *Doctor's Digest* say practices can thrive in any economy. Their advice? Follow basic business principles, embrace new modes of practice, and adopt innovative strategies to bring in revenue.

"It's not hard to manage in good times, but it is tough when times are tight," says Roland A. Goertz, MD, a family physician

The BP control and RAAS inhibition of aliskiren

The added, complementary power of amlodipine

TEKAMLO: A powerful combination for hypertension.

INDICATION

TEKAMLO is indicated for the treatment of hypertension, alone or with other antihypertensive agents.

Use TEKAMLO as initial therapy in patients who are likely to need multiple drugs to achieve their blood pressure goals. Base the choice of TEKAMLO as initial therapy on an assessment of potential benefits and risks. Individualize the decision to use a combination as initial therapy by weighing factors such as baseline blood pressure, the target goal, and the incremental likelihood of achieving goal with a combination compared to monotherapy.

Switch a patient whose blood pressure is not adequately controlled with aliskiren or amlodipine (or another dihydropyridine calcium channel blocker) alone to combination therapy with TEKAMLO.

TEKAMLO may be substituted for its titrated components.

Safety and efficacy of TEKAMLO in pediatric patients have not been established.

IMPORTANT SAFETY INFORMATION

WARNING: AVOID USE IN PREGNANCY

When pregnancy is detected, discontinue TEKAMLO as soon as possible. Drugs that act directly on the renin-angiotensin-aldosterone system can cause injury and even death to the developing fetus. See **WARNINGS and Precautions (5.1)**.

Angioedema: Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with aliskiren and has necessitated hospitalization and intubation. This may occur at any time during treatment and has occurred in patients with and without a history of angioedema with ACE inhibitors (ACEI) or angiotensin receptor antagonists. Discontinue TEKAMLO immediately in patients who develop angioedema, and do not readminister.

Hypotension: Excessive hypotension was seen rarely (0.2%) in patients with uncomplicated hypertension treated with TEKAMLO in controlled trials. Volume- and/or salt-depletion should be corrected in patients prior to administration of TEKAMLO or symptomatic hypotension may occur.

Risk of MI or Angina: Rarely, initiation or change to the dose of a calcium channel blocker has resulted in the increased frequency, duration, or severity of angina or acute myocardial infarction, particularly in patients with severe obstructive coronary artery disease.

Renal Considerations: Clinical trials with TEKAMLO and aliskiren in hypertension excluded patients with severe renal dysfunction (GFR <30 mL/min). Consider periodic determinations of serum electrolytes to detect possible imbalances.

No data are available on the use of TEKAMLO or aliskiren in patients with unilateral or bilateral renal artery stenosis. In studies of ACEIs in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen have been reported.

Hepatic Considerations: Use caution when administering TEKAMLO to patients with severe hepatic impairment, as amlodipine is extensively metabolized by the liver and the plasma elimination half-life is 56 hours in patients with impaired hepatic function.

Patients With Heart Failure: Titrate TEKAMLO slowly in patients with heart failure.

Hyperkalemia: Increases in serum potassium >5.5 mEq/L were seen (5.5%) when aliskiren was used in combination with an ACEI in hypertensive diabetic patients. Monitor electrolytes and renal function in this population. Use caution when coadministering TEKAMLO with potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, or other drugs that increase potassium levels.

Cyclosporine or Itraconazole: Avoid use of TEKAMLO with cyclosporine or itraconazole.

Furosemide: When aliskiren was coadministered with furosemide, the AUC and C_{max} of furosemide were reduced by about 30% and 50%, respectively. Patients receiving furosemide could find its effect diminished after starting aliskiren.

Common AEs: The most common adverse event in a placebo-controlled trial that occurred in at least 2% of patients treated with TEKAMLO and at a higher incidence than placebo was peripheral edema (6.2% vs 1.0%). The incidence rate of peripheral edema at high dose was 8.9%.

BP, blood pressure; RAAS, renin-angiotensin-aldosterone system.

Please see Brief Summary of Prescribing Information, including **Boxed WARNING**, on adjacent pages.



Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

© 2011 Novartis

Printed in USA

5/11

TKT-1066500



Tekamlo (aliskiren and amlodipine) tablets

Initial U.S. Approval: 2010

BRIEF SUMMARY: Please see package insert for full prescribing information.

WARNING: AVOID USE IN PREGNANCY

When pregnancy is detected, discontinue Tekamlo as soon as possible. Drugs that act directly on the renin-angiotensin-aldosterone system can cause injury and even death to the developing fetus. [See *Warnings and Precautions (5.1) and Use in Specific Populations (8.1)*].

1 INDICATIONS AND USAGE

Tekamlo is indicated for the treatment of hypertension, alone or with other antihypertensive agents.

Initial Therapy

Use Tekamlo as initial therapy in patients who are likely to need multiple drugs to achieve their blood pressure goals.

Base the choice of Tekamlo as initial therapy on an assessment of potential benefits and risks.

Add-On Therapy

Switch a patient whose blood pressure is not adequately controlled with aliskiren alone or amlodipine besylate (or another dihydropyridine calcium channel blocker) to combination therapy with Tekamlo.

Replacement Therapy

Tekamlo may be substituted for its titrated components.

Patients with moderate or severe hypertension are at a relatively high risk for cardiovascular events (such as strokes, heart attacks, and heart failure), kidney failure, and vision problems, so prompt treatment is clinically relevant. Individualize the decision to use a combination as initial therapy by weighing factors such as baseline blood pressure, the target goal, and the incremental likelihood of achieving goal with a combination compared to monotherapy. Individual blood pressure goals may vary based upon the patient's risk.

Data from the high-dose multifactorial study [see *Clinical Studies (14) in the full prescribing information*] provide estimates of the probability of reaching a target blood pressure with Tekamlo compared to aliskiren or amlodipine monotherapy. The figures below provide estimates of the likelihood of achieving systolic or diastolic blood pressure control with Tekamlo 300 mg/10 mg, based upon baseline systolic or diastolic blood pressure. The curve of each treatment group was estimated by logistic regression modeling. The estimated likelihood at the right tail of each curve is less reliable because of a small number of subjects with high baseline blood pressures.

Figure 1: Probability of Achieving Systolic Blood Pressure (SBP) <140 mmHg

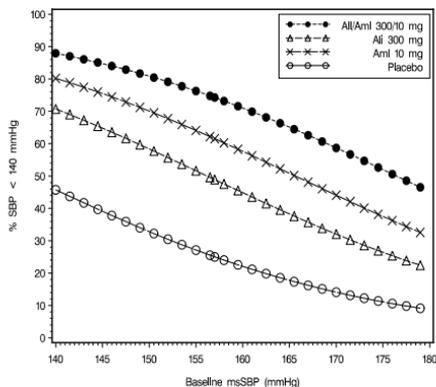


Figure 2: Probability of Achieving Diastolic Blood Pressure (DBP) <90 mmHg

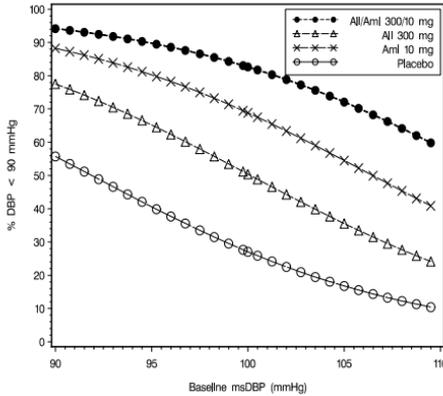


Figure 3: Probability of Achieving Systolic Blood Pressure (SBP) <130 mmHg

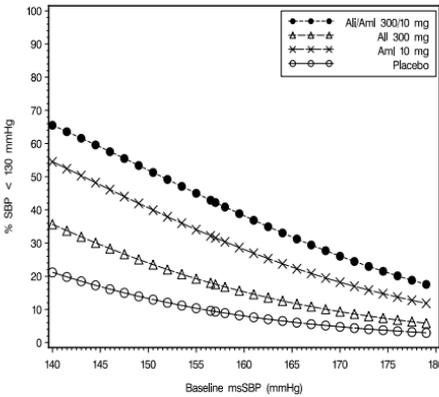
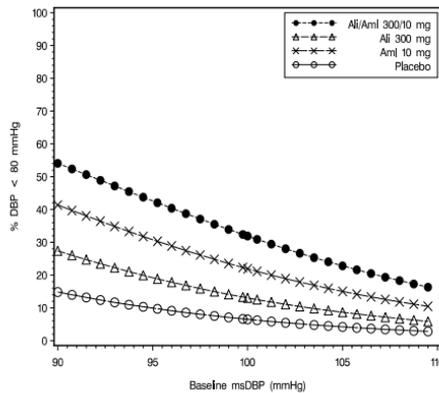


Figure 4: Probability of Achieving Diastolic Blood Pressure (DBP) <80 mmHg



The figures above provide an approximation of the likelihood of reaching a targeted blood pressure goal (e.g. SBP <140 mmHg or <130 mmHg) for the high dose groups evaluated in the study. At all levels of baseline blood pressure, the probability of achieving any given diastolic or systolic goal is greater with the combination than for either monotherapy. For example, the mean baseline SBP/DBP for patients participating in this multifactorial study was 157/100 mmHg. A patient with a baseline blood pressure of 157/100 mmHg has about a 49% likelihood of achieving a goal of <140 mmHg (systolic) and 50%

likelihood of achieving <90 mmHg (diastolic) on aliskiren alone, and the likelihood of achieving these goals on amlodipine alone is about 62% (systolic) and 69% (diastolic). The likelihood of achieving these goals on Tekamlo rises to about 74% (systolic) and 83% (diastolic). The likelihood of achieving these goals on placebo is about 25% (systolic) and 27% (diastolic) [see *Dosage and Administration (2) and Clinical Studies (14) in the full prescribing information*].

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Fetal/Neonatal Morbidity and Mortality

The use of drugs that act directly on the renin-angiotensin-aldosterone system during pregnancy can cause fetal and neonatal morbidity and death. No animal studies were conducted with Tekamlo; however, decreased fetal birth weight was observed in animal studies with aliskiren and intrauterine deaths were observed in animal studies with amlodipine. Tekamlo can cause fetal harm when administered to a pregnant woman. When pregnancy is detected, discontinue Tekamlo as soon as possible. If Tekamlo is used during pregnancy, or if a patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus [see *Use in Specific Populations (8.1)*].

5.2 Head and Neck Angioedema

Aliskiren

Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with aliskiren and has necessitated hospitalization and intubation. This may occur at any time during treatment and has occurred in patients with and without a history of angioedema with ACE inhibitors or angiotensin receptor antagonists. If angioedema involves the throat, tongue, glottis or larynx, or if the patient has a history of upper respiratory surgery, airway obstruction may occur and be fatal. Patients who experience these effects, even without respiratory distress, require prolonged observation, since treatment with antihistamines and corticosteroids may not be sufficient to prevent respiratory involvement. Prompt administration of subcutaneous epinephrine solution 1:1000 (0.3 to 0.5 ml) and measures to ensure a patent airway may be necessary.

Discontinue Tekamlo immediately in patients who develop angioedema and do not readminister.

5.3 Hypotension

An excessive fall in blood pressure (hypotension) was rarely seen (0.2%) in patients with uncomplicated hypertension treated with Tekamlo in controlled trials.

In patients with an activated renin-angiotensin-aldosterone system, such as volume- and/or salt-depleted patients receiving high doses of diuretics, symptomatic hypotension may occur in patients receiving renin-angiotensin-aldosterone system (RAAS) blockers. Correct these conditions prior to administration of Tekamlo, or start the treatment under close medical supervision.

If an excessive fall in blood pressure occurs with Tekamlo, place the patient in the supine position and, if necessary, give an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further treatment, which usually can be continued without difficulty once the blood pressure has stabilized.

5.4 Risk of Myocardial Infarction or Increased Angina

Rarely, initiation or change to the dose of a calcium channel blocker has resulted in the development of documented increased frequency, duration or severity of angina or acute myocardial infarction, particularly in patients with severe obstructive coronary artery disease. The mechanism of this effect has not been elucidated.

5.5 Impaired Renal Function

Tekamlo

Clinical trials with Tekamlo in hypertension excluded patients with severe renal impairment.

Aliskiren

Clinical trials of aliskiren in hypertension excluded patients with severe renal dysfunction (creatinine 1.7 mg/dL for women and 2.0 mg/dL for men and/or estimated GFR <30 ml/min), a history of dialysis, nephrotic syndrome, or renovascular hypertension. Consider periodic determinations of serum electrolytes to detect possible electrolyte imbalances.

5.6 Patients with Hepatic Impairment

Amlodipine besylate

Amlodipine is extensively metabolized by the liver and the plasma elimination half-life is 56 hours in patients with impaired hepatic function, therefore, caution should be exercised when administering Tekamlo to patients with severe hepatic impairment.

5.7 Patients with Congestive Heart Failure

Amlodipine besylate

Amlodipine (5-10 mg per day) has been studied in a placebo-controlled trial of 1153 patients with NYHA Class III or IV heart failure on stable doses of ACE inhibitor, digoxin, and diuretics. Follow-up was at least 6 months, with a mean of about 14 months. There was no overall adverse effect on survival or cardiac morbidity (as defined by life-threatening arrhythmia, acute myocardial infarction, or hospitalization for worsened heart failure). Amlodipine has been compared to placebo in four 8-12 week studies of patients with NYHA Class II/III heart failure, involving a total of 697 patients. In these studies, there was no evidence of worsened heart failure based on measures of exercise tolerance, NYHA classification, symptoms, or left ventricular ejection fraction.

5.8 Renal Artery Stenosis

No data are available on the use of Tekamlo or aliskiren in patients with unilateral or bilateral renal artery stenosis or stenosis of the artery to a solitary kidney. However, in studies of ACE inhibitors in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen have been reported.

5.9 Cyclosporine or Itraconazole

Aliskiren

When aliskiren was given with cyclosporine or itraconazole, the blood concentrations of aliskiren were significantly increased. Avoid concomitant use of aliskiren with cyclosporine or itraconazole [see *Drug Interactions (7)*].

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

The following serious adverse reactions are discussed in greater detail in other sections of the label:

- Risk of fetal/neonatal morbidity and mortality [see *Warnings and Precautions (5.1)*]
- Head and neck angioedema [see *Warnings and Precautions (5.2)*]
- Hypotension [see *Warnings and Precautions (5.3)*]

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in clinical trials of another drug and may not reflect the rates observed in practice.

Tekamlo

Tekamlo has been evaluated for safety in more than 2800 patients, including 372 patients for 1 year or longer.

In a placebo-controlled study, there were 51% males, 62% Caucasians, 20% Blacks, 18% Hispanics, and 17% who were over 65 years of age. In this study, the overall incidence of adverse events on therapy with Tekamlo was similar to the individual components. Discontinuation of therapy due to a clinical adverse event in this study occurred in 1.7% of patients treated with Tekamlo (2.2% in the highest dose group) versus 1.5% of patients given placebo.

Peripheral edema is a known, dose-dependent adverse effect of amlodipine. The incidence of peripheral edema for Tekamlo in short-term double-blind placebo-controlled studies was lower than or equal to that of the corresponding amlodipine doses.

The adverse event in a placebo-controlled trial that occurred in at least 2% of patients treated with Tekamlo and at a higher incidence than placebo was peripheral edema (6.2% versus 1.0%). The incidence rate of peripheral edema at high dose was 8.9%.

In a long-term safety trial, the safety profile of adverse events was similar to that seen in the short-term controlled trials.

Aliskiren

Aliskiren has been evaluated for safety in 6460 patients, including 1740 treated for longer than 6 months, and 1250 for longer than 1 year. In placebo-controlled clinical trials, discontinuation of therapy because of a clinical adverse event, including uncontrolled hypertension, occurred in 2.2% of patients treated with aliskiren versus 3.5% of patients given placebo.

Two cases of angioedema with respiratory symptoms were reported with aliskiren use in the clinical studies. Two other cases of periorbital edema without respiratory symptoms were reported as possible angioedema and resulted in discontinuation. The rate of these angioedema cases in the completed studies was 0.06%.

In addition, 26 other cases of edema involving the face, hands, or whole body were reported with aliskiren use, including 4 leading to discontinuation.

In the placebo-controlled studies, however, the incidence of edema involving the face, hands, or whole body was 0.4% with aliskiren compared with 0.5% with placebo. In a long-term active-controlled study with aliskiren and HCTZ arms, the incidence of edema involving the face, hands, or whole body was 0.4% in both treatment arms.

Aliskiren produces dose-related gastrointestinal (GI) adverse reactions. Diarrhea was reported by 2.3% of patients at 300 mg, compared to 1.2% in placebo patients. In women and the elderly (age ≥ 65) increases in diarrhea rates were evident starting at a dose of 150 mg daily, with rates for these subgroups at 150 mg similar to those seen at 300 mg for men or younger patients (all rates about 2%). Other GI symptoms included abdominal pain, dyspepsia, and gastroesophageal reflux, although increased rates for abdominal pain and dyspepsia were distinguished from placebo only at 600 mg daily. Diarrhea and other GI symptoms were typically mild and rarely led to discontinuation.

Aliskiren was associated with a slight increase in cough in the placebo-controlled studies (1.1% for any aliskiren use versus 0.6% for placebo). In active-controlled trials with ACE inhibitor (ramipril, lisinopril) arms, the rates of cough for the aliskiren arms were about one-third to one-half the rates in the ACE inhibitor arms.

Other adverse reactions with increased rates for aliskiren compared to placebo included rash (1% versus 0.3%), elevated uric acid (0.4% versus 0.1%), gout (0.2% versus 0.1%), and renal stones (0.2% versus 0%).

Single episodes of tonic-clonic seizures with loss of consciousness were reported in two patients treated with aliskiren in the clinical trials. One patient had predisposing causes for seizures and had a negative electroencephalogram (EEG) and cerebral imaging following the seizures; for the other patient, EEG and imaging results were not reported. Aliskiren was discontinued and there was no rechallenge in either case.

No clinically meaningful changes in vital signs or in ECG (including QTc interval) were observed in patients treated with aliskiren.

Amlodipine besylate

Amlodipine (Norvasc[®]) has been evaluated for safety in more than 11,000 patients in U.S. and foreign clinical trials. Other adverse events that have been reported <1% but >0.1% of patients in controlled clinical trials or under conditions of open trials or marketing experience where a causal relationship is uncertain were:

Cardiovascular: arrhythmia (including ventricular tachycardia and atrial fibrillation), bradycardia, chest pain, peripheral ischemia, syncope, postural hypotension, vasculitis

Central and Peripheral Nervous System: neuropathy peripheral, paresthesia, tremor, vertigo

Gastrointestinal: anorexia, constipation, dyspepsia, ** dysphagia, diarrhea, flatulence, pancreatitis, vomiting, gingival hyperplasia

General: allergic reaction, asthenia, ** back pain, hot flushes, malaise, pain, rigors, weight gain, weight decrease

Musculoskeletal System: arthralgia, arthrosis, muscle cramps, ** myalgia

Psychiatric: sexual dysfunction (male** and female), insomnia, nervousness, depression, abnormal dreams, anxiety, depersonalization

Respiratory System: dyspnea, epistaxis

Skin and Appendages: angioedema, erythema multiforme, pruritus, ** rash, ** rash erythematous, rash maculopapular

*These events occurred in less than 1% in placebo-controlled trials, but the incidence of these side effects was between 1% and 2% in all multiple dose studies.

Special Senses: abnormal vision, conjunctivitis, diplopia, eye pain, tinnitus

Urinary System: micturition frequency, micturition disorder, nocturia

Autonomic Nervous System: dry mouth, sweating increased

Metabolic and Nutritional: hyperglycemia, thirst

Hemopoietic: leukopenia, purpura, thrombocytopenia

Other events reported with amlodipine at a frequency of $\leq 0.1\%$ of patients include: cardiac failure, pulse irregularity, extrasystoles, skin discoloration, urticaria, skin dryness, alopecia, dermatitis, muscle weakness, twitching, ataxia, hypertonia, migraine, cold and clammy skin, apathy, agitation, amnesia, gastritis, increased appetite, loose stools, rhinitis, dysuria, polyuria, parosmia, taste perversion, abnormal visual accommodation, and xerophthalmia. Other reactions occurred sporadically and cannot be distinguished from medications or concurrent disease states such as myocardial infarction and angina.

6.2 Clinical Laboratory Test Abnormalities

RBC count, hemoglobin and hematocrit: Small mean changes from baseline were seen in RBC count, hemoglobin and hematocrit in patients treated with both Tekamlo and aliskiren monotherapy. This effect is also seen with other agents acting on the renin-angiotensin system. In aliskiren monotherapy trials these decreases led to slight increases in rates of anemia compared to placebo (0.1% for any aliskiren use, 0.3% for aliskiren 600 mg daily, vs. 0% for placebo). No patients discontinued due to anemia.

Blood Urea Nitrogen (BUN)/Creatinine: Elevations in BUN (>40 mg/dL) and creatinine (>2.0 mg/dL) in patients treated with Tekamlo were <1.0%.

Serum Potassium: Increases in serum potassium >5.5 mEq/L were infrequent in patients with essential hypertension treated with both Tekamlo and aliskiren monotherapy (0.9% compared to 0.6% with placebo). However, when aliskiren was used in combination with an angiotensin-converting enzyme inhibitor (ACEI) in a diabetic population, increases in serum potassium were more frequent (5.5%). Monitor electrolytes and renal function in this population.

6.3 Post-marketing Experience

The following adverse reactions have been identified during postapproval use of either aliskiren or amlodipine. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency or establish a causal relationship to drug exposure:

Hypersensitivity: angioedema requiring airway management and hospitalization

Aliskiren: Peripheral edema, blood creatinine increased

Amlodipine: The following postmarketing event has been reported infrequently where a causal relationship is uncertain: gynecomastia. In postmarketing experience, jaundice and hepatic enzyme elevations (mostly consistent with cholestasis or hepatitis), in some cases severe enough to require hospitalization, have been reported in association with use of amlodipine.

7 DRUG INTERACTIONS

No drug interaction studies have been conducted with Tekamlo and other drugs, although studies with the individual aliskiren and amlodipine besylate components are described below.

Aliskiren

Cyclosporine: Avoid co-administration of cyclosporine with aliskiren.

Itraconazole: Avoid co-administration of itraconazole with aliskiren.

[See Clinical Pharmacology (12.3) in the full prescribing information.]

Amlodipine besylate

In clinical trials, amlodipine has been safely administered with thiazide diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, long-acting nitrates, sublingual nitroglycerin, digoxin, warfarin, non-steroidal anti-inflammatory drugs, antibiotics, and oral hypoglycemic drugs.

Cimetidine: Co-administration of amlodipine with cimetidine did not alter the pharmacokinetics of amlodipine.

Grapefruit juice: Co-administration of 240 mL of grapefruit juice with a single oral dose of amlodipine 10 mg in 20 healthy volunteers had no significant effect on the pharmacokinetics of amlodipine.

Maalox[®] (antacid): Co-administration of the antacid Maalox with a single dose of amlodipine had no significant effect on the pharmacokinetics of amlodipine.

Sildenafil: A single 100 mg dose of sildenafil in subjects with essential hypertension had no effect on the pharmacokinetic parameters of amlodipine. When amlodipine and sildenafil were used in combination, each agent independently exerted its own blood pressure lowering effect.

Atorvastatin: Co-administration of multiple 10 mg doses of amlodipine with 80 mg of atorvastatin resulted in no significant change in the steady-state pharmacokinetic parameters of atorvastatin.

Digoxin: Co-administration of amlodipine with digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers.

Ethanol (alcohol): Single and multiple 10 mg doses of amlodipine had no significant effect on the pharmacokinetics of ethanol.

Warfarin: Co-administration of amlodipine with warfarin did not change the warfarin prothrombin response time.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category D [See Warnings and Precautions Section]

The use of drugs that act directly on the renin-angiotensin-aldosterone system during the second and third trimesters of pregnancy can cause fetal and neonatal morbidity and death. In addition, first trimester use of ACE inhibitors has been associated with birth defects in retrospective data. No animal studies were

conducted with Tekamlo; however, decreased fetal birth weight was observed in animal studies with aliskiren and intrauterine deaths were observed in animal studies with amlodipine. Tekamlo can cause fetal harm when administered to a pregnant woman. When pregnancy is detected, discontinue Tekamlo as soon as possible. If Tekamlo is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Human Data and Clinical Considerations

Maternal hypertension is associated with increased risks for preterm delivery, intrauterine growth restriction, placental abruption, preeclampsia, and perinatal mortality. Appropriate management of maternal hypertension during pregnancy is important to optimize outcomes for both mother and fetus. Renin inhibitors (like aliskiren), angiotensin II receptor antagonists and angiotensin converting enzyme (ACE) inhibitors exert similar effects on the renin-angiotensin-aldosterone system. Based on several dozen published cases, ACE inhibitor use during the second and third trimesters of pregnancy is associated with fetal and neonatal injury, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Decreased fetal renal function may result in oligohydramnios and associated with fetal limb contractures, craniofacial deformation, and hypoplastic lung development. Prematurity, intrauterine growth retardation, and patent ductus arteriosus have been reported in women using these drugs, but it is not clear whether these occurrences were due to drug exposure. Limited data are conflicting about whether first trimester use of ACE inhibitors is associated with an increased risk of birth defects, but the drugs' mechanism of action raises a theoretical concern.

When pregnancy occurs in a patient using Tekamlo, the physician should discontinue Tekamlo treatment as soon as possible. Inform the patient about potential risks to the fetus based on the time of gestational exposure to Tekamlo (first trimester only or later). If exposure occurs beyond the first trimester, perform an ultrasound examination.

In rare cases when another antihypertensive agent cannot be used to treat the pregnant patient, serial ultrasound examinations should be used to assess the intraamniotic environment. Routine fetal testing with non-stress tests, biophysical profiles, and/or contraction stress tests may be appropriate based on gestational age and standards of care in the community. If oligohydramnios occurs in these situations, individualized decisions about continuing or discontinuing Tekamlo treatment and about pregnancy management should be made by the patient and her physicians. Patients and physicians should be aware that oligohydramnios may not appear until after the fetus has sustained irreversible injury.

Infants exposed to Tekamlo in-utero should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, these infants may require blood pressure and renal perfusion support. Exchange transfusion or dialysis may be required to reverse hypotension and/or support decreased renal function.

Animal Data

No reproductive toxicity studies have been conducted with the combination of aliskiren and amlodipine besylate. However, these studies have been conducted for aliskiren and amlodipine besylate alone.

Aliskiren

In developmental toxicity studies, pregnant rats and rabbits received oral aliskiren hemifumarate during organogenesis at doses up to 20 and 7 times the maximum recommended human dose (MRHD) based on body surface area (mg/m^2), respectively, in rats and rabbits. (Actual animal doses were up to 600 $\text{mg}/\text{kg}/\text{day}$ in rats and up to 100 $\text{mg}/\text{kg}/\text{day}$ in rabbits.) No teratogenicity was observed; however, fetal birth weight was decreased in rabbits at doses 3.2 times the MRHD based on body surface area (mg/m^2). Aliskiren was present in placentas, amniotic fluid and fetuses of pregnant rabbits.

Amlodipine

In developmental toxicity studies, pregnant rats and rabbits received oral amlodipine maleate during organogenesis at doses approximately 10 and 20 times the maximum recommended human dose (MRHD) based on body surface area (mg/m^2), respectively, in rats and rabbits. (Actual animal doses were up to 10 $\text{mg}/\text{kg}/\text{day}$.) No evidence of teratogenicity or other embryofetal toxicity was observed. However, litter size was decreased approximately 50% and the number of intrauterine deaths was increased approximately 5-fold for rats receiving amlodipine maleate at doses approximately 10 times the MRHD based on body surface area (mg/m^2) for 14 days before mating and throughout mating and gestation. Amlodipine maleate has been shown to prolong both the gestation period and the duration of labor in rats at this dose.

8.3 Nursing Mothers

It is not known whether aliskiren or amlodipine is excreted in human milk. Both aliskiren and amlodipine are secreted in the milk of lactating rats. Because of the potential for serious adverse reactions in human milk-fed infants from Tekamlo, a decision should be made whether to discontinue nursing or discontinue Tekamlo, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness of Tekamlo in pediatric patients have not been established.

8.5 Geriatric Use

Tekamlo

In the short-term controlled clinical trials of Tekamlo, 17% of patients treated with Tekamlo were ≥ 65 years. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Aliskiren

Impact of aging on aliskiren pharmacokinetics has been assessed, when compared to young adults (18-40 years), aliskiren mean AUC and C_{max} in elderly subjects (>65 years) are increased by 57% and 28%, respectively. However, differences in efficacy and safety between the elderly and younger populations were minor, indicating that differences in exposure due to age do not significantly alter the clinical effect of the drug. Therefore, no starting dose adjustment in geriatric population is required.

Amlodipine

Other reported clinical experience has not identified differences in responses between the elderly and younger patients. However, elderly patients have decreased clearance of amlodipine with a resulting increase of AUC of approximately 40-60%. In general dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

10 OVERDOSAGE

Aliskiren

Limited data are available related to overdosage in humans. The most likely manifestation of overdosage would be hypotension. If symptomatic hypotension should occur, provide supportive treatment.

Amlodipine besylate

Single oral doses of amlodipine maleate equivalent to 40 mg amlodipine/kg and 100 mg amlodipine/kg in mice and rats, respectively, caused deaths. Single oral amlodipine maleate doses equivalent to 4 or more mg amlodipine/kg or higher in dogs (11 or more times the maximum recommended human dose on a mg/m^2 basis) caused a marked peripheral vasodilation and hypotension.

Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotension and possibly a reflex tachycardia. In humans, experience with intentional overdosage of amlodipine is limited. Reports of intentional overdosage include a patient who ingested 250 mg and was asymptomatic and was not hospitalized; another (120 mg) was hospitalized, underwent gastric lavage and remained normotensive; the third (105 mg) was hospitalized and had hypotension (90/50 mmHg) which normalized following plasma expansion. A case of accidental drug overdose has been documented in a 19-month-old male who ingested 30 mg amlodipine (about 2 mg/kg). During the emergency room presentation, vital signs were stable with no evidence of hypotension, but a heart rate of 180 bpm. Ipecac was administered 3.5 hours after ingestion and on subsequent observation (overnight) no sequelae were noted.

If massive overdose should occur, active cardiac and respiratory monitoring should be instituted. Frequent blood pressure measurements are essential. Should hypotension occur, cardiovascular support including elevation of the extremities and the judicious administration of fluids should be initiated. If hypotension remains unresponsive to these conservative measures, administration of vasopressors (such as phenylephrine) should be considered with attention to circulating volume and urine output. Intravenous calcium gluconate may help to reverse the effects of calcium entry blockade. As amlodipine is highly protein bound, hemodialysis is not likely to be of benefit.

Distributed by:
Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936

T2011-52
March 2011

©Novartis

in Waco, Tex., and president of the American Academy of Family Physicians (AAFP). “Now that margins are slimmer and resources are tighter, you have to pay more attention to the details of efficiency and the cost side. That’s something that a lot of physicians can learn to do better.”



“[Most physicians] go into the office every day; and if there’s money at the end of the month, they have a salary—that’s not a plan.”

Michael La Penna
Principal
The La Penna Group
Grand Rapids, Mich.

In this issue of *Doctor’s Digest*, we take a look at what it takes to be financially successful as a primary care physician. Experts weigh in on the fundamentals of budgeting and forecasting, boosting cash flow, and adopting smart staffing practices. We talk to financially successful physicians who explain their business philosophy and best practices, from offering ancillary services to adopting innovative business models. These successful physicians share not only an appreciation for the business side of medicine, but also an openness to making the innovations that keep patients coming through the door year after year.

The Revenue Pyramid

Recent surveys reveal that many specialists make significantly more money than family physicians, general internists, or pediatricians. The Medical Group Management Association’s (MGMA) *2010 Physician Compensation and Production Survey* (based on 2009 data) found that while the three primary care specialties’ median compensation was under \$200,000, the figure is much higher for other specialists, such as hematologists/oncologists (\$369,000), diagnostic radiologists (\$479,000), and invasive cardiologists (\$482,000).

“A change in payment methodology is essential,” Dr. Goertz says. “The current [fee-for-service] model does not allow a prac-



American Medical Women's Association
The Vision and Voice of Women in Medicine since 1915

Join Today!

Visit our website, www.amwa-doc.org or email associatedirector@amwa-doc.org for information on membership.

Physicians, medical students, residents and non-medical professionals are all welcome.

tice to use creative or innovative ways to care for patients unless a code already exists for the services—no code, no payment. We need a system of payment that rewards the most appropriate care and services, one that rewards good coordination of care with other specialists, and for improving communications about services.” AAFP and other major medical groups are pushing for an overhaul of fee-for-service in conjunction with pilot programs and grants, and back compensating physicians for coordinating care and implementing principles of the patient-centered medical home (PCMH). See “The Promise of Healthcare Reform.”

Even without payment reform, however, Dr. Goertz says it makes good business sense for practices to invest in new technologies, such as electronic health records (EHRs), and implement improvements that lead to better quality and efficiency. “Outlaying some investment upfront is worth it in the long run,” says Dr. Goertz, who is CEO of the three foundations that oversee the Waco Family Health Center in Waco, Texas.

Embracing the Business of Medicine

Practices don't have to overhaul themselves to have a positive impact on their bottom lines today, instead finding benefits from shoring up practice finances and management structures, says Michael La Penna, principal of the La Penna Group, a healthcare strategic and financial consulting service based in Grand Rapids, Mich. He says doing so is particularly important for primary care physicians, who must deal with the same rising costs (staff salaries, office rent, etc.) and flawed reimbursement system as

The Promise of Healthcare Reform

Practices that budget, plan ahead, and invest for the future not only tend to profit in the short-term but will be poised to surge ahead when health reform becomes a reality. A major focus of the Affordable Care Act (ACA) is to strengthen primary care by rewarding physicians for innovative, progressive ways of delivering care that lead to better overall outcomes for patients.

The ACA began to benefit primary care physicians this year, with a five-year 10% Medicare payment bonus for physicians whose primary care services equal at least 60% of their total Medicare revenue (qualifying primary care services must fall under certain billing codes relating to office/outpatient visits, nursing facility services, custodial care services, and home services).

In its September 2010 report, "An Internist's Practical Guide to Understanding Health System Reform," the ACP estimates that a typical general internist who brings in \$200,000 in annual Medicare revenue and qualifies for the bonus program would receive an additional \$12,000 a year, based on meeting the 60% threshold. Internists whose qualifying primary care billings reach 80% of Medicare revenue would earn \$16,000 per bonus year, or \$80,000 over the five-year program.

Health reform would also benefit physicians who adopt the PCMH model by allowing states to increase reimbursement for practices designated as "health homes" for Medicaid patients with chronic conditions, according

more highly paid specialists but with fewer resources. Added to that is the increasing pressure to invest in technology.

"It's a perfect storm of reimbursement woes, cost structures of all things medical increasing, and an immediate need to transition the way [primary care physicians] practice and invest in capital equipment like EHRs," he says.

The best response in this challenging financial environment is to develop a well-thought-out plan. Unfortunately, most physicians don't have one. "They go into the office every day; and if there's money at the end of the month, they have a salary—that's not a plan," Mr. La Penna says. "They've got to have a vision of where they fit into the marketplace and how their practice fits into the scheme of all these things that are being played out." Those positive options include paying more attention to the important role of primary care physicians in coordinating care, to low interest rates that favor investment, and to the higher-

to the Commonwealth Fund's January 2011 report, "Realizing Health Reform's Potential." The report lists other provisions of the law that impact primary care, including these:

- Increased Medicaid reimbursement for primary care to at least Medicare levels in 2013 and 2014
- Reduction in uncompensated care due to 32 million more people's being insured with preventive and primary care coverage
- Support for Medicare and Medicaid PCMH pilots
- Support for medical homes through funding for community health teams, community collaborative-care networks for low-income populations, and the Primary Care Extension Center program offering technical assistance for providers
- Scholarships, loan repayment, and training programs for primary care physicians and mid-level and community providers
- \$11 billion for federally qualified health centers in 2011 and continuing through 2015

For more information about the impact of healthcare reform on your practice, see *Preparing for Healthcare Reform*, *Doctor's Digest's* May/June 2011 issue, at <http://www.doctorsdigest.net/issue/0703.php>.

quality and more affordable EHRs customized for primary care.

Instead, he says, primary care physicians tend to be reactive instead of proactive (e.g., formulating a plan for investing their money and time) when making business decisions. If a nearby hospital suggests an affiliation, for example, the reactive physician may simply accept without researching other options or talking to other hospitals. "It's called serial incident planning—making mini-plans based on every sales call or negotiation," he

New Job Resource for Healthcare Professionals Only

Find a job or post an opening on **HCP Exchange**,™ *Doctor's Digest's* new **free** employment service. Go to www.doctorsdigest.net and click on **HCP Exchange**™, or download our FREE MEDICAL Practice Management iPad App: *Doctor's Digest Practice Solution Center*™.



explains. “If you have no business plan, you are just going to be buffeted by other business plans that are more pronounced. But there’s no potential for stabilizing your practice long-term.”



“We see technology as enhancing the relationship, allowing the development of a strong physician-patient relationship. These things [i.e., stronger physician-patient relationships and easy access to services] are foundational to having a practice that will generate revenue.”

Steve Rallison
COO
Greenfield Health
Portland, Ore.

The first step for doctors who don’t budget and forecast in any formal way is to go back to—or relearn—business basics, says Margo Williams, senior associate in the American College of Physicians (ACP) Center for Practice Improvement and Innovation. “Practice Finance for Physicians 101,” a popular ACP workshop co-led by Ms. Williams, starts with topics ranging from balancing a checkbook to collecting on claims. Consultants at TransforMED, a subsidiary of AAFP, are often struck by the lack of formal planning or budgeting in small practices, says James L. Arend, MBA, chief financial and operating officer of TransforMED. “We expect [physicians] to understand basic business principles, but their business acumen usually isn’t where it needs to be,” he says. “First and foremost they are physicians, but they also need to be business people.” (See “Advice for New Practices.”)

Investing in Technology

Following sound business practices, such as formal budgeting, forecasting, and benchmarking, is a good foundation for profitability, but it’s only a beginning. Successful businesses also must invest in order to grow. For medical practices, a key move is to join the rest of the business world in using technology to

Advice for New Practices

New practices that find themselves in trouble financially often don't understand their cash flow, says Jeffrey Milburn, a Colorado Springs-based consultant for MGMA. As a result, they don't anticipate their true costs starting out and end up running out of cash unexpectedly.

"When you open up, you're hit with low patient volume initially, delayed cash collections from billings—some providers don't understand how long it takes to collect from insurers—and expenses are immediate," Mr. Milburn says. In order to offset their front-end expenses for equipment, marketing, and other start-up needs while paying their monthly rent and salaries, physicians often have to rely on personal savings or bank loans, he adds.

Here are some tips for starting out right:

- Make sure you have savings or loans in place to cover fixed expenses in the first year while you are growing your clientele.
- Create a month-by-month cash flow spreadsheet so you can estimate when you might need to dip into personal savings or loans.
- Using an average office visit charge, calculate how many patients you will need to see per day to turn a profit; and estimate how long it will take to reach that goal.
- Remember to budget for marketing expenses to attract new patients.
- Secure contracts with government and private payers before you open, as it can take months to get credentialed with some payers.

streamline their operations and improve customer service. There is a connection among use of technology, high level of service, and quality of care, says Steve Rallison, COO of Portland, Ore.-based Greenfield Health, where physicians' extensive use of e-mail and secure messaging allows them to spend more time with complex patients in the exam room. "Easy access and rapid response to patients' needs engender mutual respect and trust, which allow the [physician-patient] relationship to occur," says Mr. Rallison. "We see technology as enhancing the relationship, allowing the development of a strong physician-patient relationship. These things [i.e., stronger physician-patient relationships and easy access to services] are foundational to having a practice that will generate revenue."

Currently, about 62% of AAFP members use EHRs in some

capacity, says Terry McGeeney, MD, CEO of TransformMED. While most physicians plan to convert from paper, many still view EHRs as a new way of documenting information rather than an enhancement of their ability to conduct business and hence a way to improve their bottom line. “We try to get them to understand that if they leverage all of the uses [of EHRs], there are a lot of ways to increase revenue and reduce overhead,” he says. For example, practices no longer need a separate room for paper files, nor do they need a staff member dedicated to filing. In addition, EHR systems can help increase visits by sending out electronic reminders for routine care and follow-up visits.

Just as practices need a business plan, they also need a technology plan that includes a timeline for conversion to new technologies, one that also details the types of components they will need. An initial report on the AAFP’s PCMH demonstration project, published in *Annals of Family Medicine* (2009;7:254-260), recommends that practices revise and update their plan frequently to reflect emerging technology and their practice’s specific needs.

Can Solo Practices Survive?

With so much pressure to invest in new systems and adopt innovative models, many wonder whether the solo practice—which accounts for about one-third of primary care practices—is a dying entity. Many practices have chosen to ally with deeper-pocketed partners, such as hospitals and large medical groups, a trend that is reflected in the changing composition of AAFP’s membership, Dr. Goertz says. AAFP now represents as many physicians from large practices or employment settings as from small- to medium-size practices, a significant change from the past when it was heavily weighted toward smaller practices, he notes.

But Dr. Goertz and other practice management experts contend that smaller practices can successfully navigate the new healthcare landscape if they are open to new ways of practicing and doing business, ways that can help small practices grow while maintaining control over what is most important to them: patient-physician interaction. For example, he says, innovative practices can do the following:

- Align with each other to purchase technology or services
- Improve patient flow and efficiency by partnering with nurse practitioners (NPs) and physician assistants (PAs) in order to free the physician to concentrate on complex patient care
- Adopt innovative models of care, such as group visits
- Join with other practices to purchase services or implement technology

A recent report from the Commonwealth Fund, *2009 Commonwealth Fund International Health Policy Survey of Primary Care Physicians*, notes that the ACA supports the shared-resources model by funding community health teams to support the PCMH model, primary care extension programs for technical assistance, and community-based networks that assist low-income patients' access to care. These new resources and financial alliances will help the solo practitioner form financial alliances in order to remain clinically independent.

“Back in the mid-1990s, when big groups were buying up small practices, people thought that would be the end of the solo practitioner; but it wasn't, and I don't think it is now,” says Jeffrey Milburn, a Colorado Springs-based consultant for MGMA.

Get *Doctor's Digest* Interactive on Your iPad

Don't miss our new Digital Editions featuring expert advice, real time-ISMP

Medication and Hazard Alerts, personal finance tips, and much more.

Now available in our **FREE MEDICAL** Practice Management iPad App:

Doctor's Digest Practice Solution Center[™].

