Table 1 Adverse Events Reported by 2% or More of Pediatric Patients Taking Vyvanse in a 4 Week Clinical Trial

Body System	Preferred Term	Vyvanse (n=218)	Placebo (n=72)
Gastrointestinal Disorders	Abdominal Pain Upper	12%	6%
	Dry Mouth	5%	0%
	Nausea	6%	3%
	Vomiting	9%	4%
General Disorder and Administration Site Conditions	Pyrexia	2%	1%
Investigations	Weight Decreased	9%	1%
Metabolism and Nutrition	Decreased Appetite	39%	4%
Nervous System Disorders	Dizziness	5%	0%
	Headache	12%	10%
	Somnolence	2%	1%
Psychiatric Disorders	Affect lability	3%	0%
	Initial Insomnia	4%	0%
	Insomnia	19%	3%
	Irritability	10%	0%
	Tic	2%	0%
Skin and Subcutaneous Tissue Disorders	Rash	3%	0%

Note: This table only includes those events for which the incidence in patients taking Vyvanse is greater than the incidence in patients taking placebo.

The following additional adverse reactions have been associated with the use of amphetamine, amphetamine (d to l enantiomer ratio of 3:1), or Vyvanse:

Cardiovascular: Palpitations, tachycardia, elevation of blood pressure, sudden death, myocardial infarction. There have been isolated reports of cardiomyopathy associated with chronic amphetamine use.

Central Nervous System: Psychotic episodes at recommended doses, overstimulation, restlessness, dizziness, euphoria, dyskinesia, dysphoria, depression, tremor, headache, exacerbation of motor and phonic tics and Tourette's syndrome, seizures, stroke.

Gastrointestinal: Dryness of the mouth, unpleasant taste, diarrhea, constipation.

Allergic: Urticaria, hypersensitivity reactions including angioedema and anaphylaxis. Serious skin rashes, including Stevens Johnson Syndrome and toxic epidermal necrolysis have been reported.

Endocrine: Impotence, changes in libido.

DRUG ABUSE AND DEPENDENCE

Controlled Substance Class

Vyvanse is classified as a Schedule II controlled substance.

Amphetamines have been extensively abused. Tolerance, extreme psychological dependence, and severe social disability have occurred. There are reports of patients who have increased the dosage to levels many times higher than recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with amphetamines may include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

Human Studies
In a human abuse liability study, when equivalent oral doses of 100 mg lisdexamfetamine dimesylate and 40 mg immediate release d-amphetamine sulfate were administered to individuals with a history of drug abuse, lisdexamfetamine 100 mg produced subjective responses on a scale of "Drug Liking Effects" "Amphetamine Effects", and "Stimulant Effects" that were significantly less than d-amphetamine immediate release 40 mg. However, oral administration of 150 mg lisdexamfetamine produced increases in positive subjective responses on these scales that were statistically indistinguishable from the positive subjective responses produced by 40 mg of oral immediate-release d-amphetamine and 200 mg of diethylpropion (C-IV).

Intravenous administration of 50 mg lisdexamfetamine to individuals with a history of drug abuse produced positive subjective responses on scales measuring "Drug Liking", "Euphoria", "Amphetamine Effects", and "Benzedrine Effects" that were greater than placebo but less than those produced by an equivalent dose (20 mg) of intravenous d-amphetamine.

Animal Studies
In animal studies, lisdexamfetamine produced behavioral effects qualitatively similar to those of the CNS stimulant d-amphetamine. In monkeys trained to self-administer cocaine, intravenous lisdexamfetamine maintained self-administration at a rate that was statistically less than that for cocaine, but greater than that of placebo.

OVERDOSAGE

Individual response to amphetamines varies widely. Toxic symptoms may occur idiosyncratically at low doses.

Symptoms: Manifestations of acute overdosage with amphetamines include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states, hyperpyrexia and rhabdomyolysis. Fatigue and depression usually follow the central nervous system stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension

and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning is usually preceded by convulsions and coma.

Treatment: Consult with a Certified Poison Control Center for up to date guidance and advice. Management of acute amphetamine intoxication is largely symptomatic and includes gastric lavage, administration of activated charcoal, administration of a cathartic and sedation. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Acidification of the urine increases amphetamine excretion, but is believed to increase risk of acute renal failure if myoglobinuria is present. If acute severe hypertension complicates amphetamine overdosage, administration of intravenous phentolamine has been suggested. However, a gradual drop in blood pressure will usually result when sufficient sedation has been achieved. Chlorpromazine antagonizes the central stimulant effects of amphetamines and can be used to treat amphetamine intoxication.

The prolonged release of Vyvanse in the body should be considered when treating patients with overdose.

DOSAGE AND ADMINISTRATION

Dosage should be individualized according to the therapeutic needs and response of the patient. Vyvanse should be administered at the lowest effective dosage.

In children with ADHD who are 6-12 years of age and are either starting treatment for the first time or switching from another medication, 30 mg once daily in the morning is the recommended dose. If the decision is made to increase the dose beyond 30 mg/day, daily dosage may be adjusted in increments of 20 mg/day and at approximately weekly intervals. The maximum recommended dose for children is 70 mg/day; doses greater than 70 mg/day of Vyvanse have not been studied in children. Amphetamines are not recommended for children under 3 years of age. Vyvanse has not been studied in children under 6 or over 12 years of age.

Vyvanse should be taken in the morning. Afternoon doses should be avoided because of the potential for insomnia.

Vyvanse may be taken with or without food.

Vyvanse capsules may be taken whole, or the capsule may be opened and the entire contents dissolved in a glass of water. If the patient is using the solution administration method, the solution should be consumed immediately; it should not be stored. The dose of a single capsule should not be divided. The contents of the entire capsule should be taken, and patients should not take anything less than one capsule per day.

Where possible, drug administration should be interrupted occasionally to determine if there is a recurrence of behavioral symptoms sufficient to require continued therapy.

HOW SUPPLIED

Vyvanse capsules 30 mg: white body/orange cap (imprinted NRP104 30 mg), bottles of 100, NDC 59417-103-10

Vyvanse capsules 50 mg: white body/blue cap (imprinted NRP104 50 mg), bottles of 100, NDC 59417-105-10

Vyvanse capsules 70 mg: blue body/orange cap (imprinted NRP104 70 mg), bottles of 100, NDC 59417-107-10

Dispense in a tight, light-resistant container as defined in the USP.

Store at 25° C (77° F). Excursions permitted to 15 - 30° C (59-86° F) [see USP Controlled Room Temperature]

ANIMAL TOXICOLOGY

Acute administration of high doses of amphetamine (d- or d,l-) has been shown to produce long-lasting neurotoxic effects, including irreversible nerve fiber damage, in rodents. The significance of these findings to humans is unknown.

Manufactured for: New River Pharmaceuticals Inc., Blacksburg, VA 24060. Made in USA.

Distributed by: Shire US Inc., Wayne, PA 19087

For more information call 1-800-828-2088, or visit www.Vyvanse.com

Vyvanse is a trademark of Shire LLC.

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MEDICATION GUIDE
VYVANSE™
(lisdexamfetamine dimesylate) CII

Read the Medication Guide that comes with Vyvanse before you or your child starts taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your doctor about you or your child's treatment with Vyvanse.

What is the most important information I should know about Vyvanse?

Vyvanse is a stimulant medicine. The following have been reported with use of stimulant medicines.

1. Heart-related problems:

- **sudden death in patients who have heart problems or heart defects**
- **stroke and heart attack in adults**
- **increased blood pressure and heart rate**

Tell your doctor if you or your child have any heart problems, heart defects, high blood pressure, or a family history of these problems.

Your doctor should check you or your child carefully for heart problems before starting Vyvanse.

Your doctor should check you or your child's blood pressure and heart rate regularly during treatment with Vyvanse.

Call your doctor right away if you or your child has any signs of heart problems such as chest pain, shortness of breath, or fainting while taking Vyvanse.

2. Mental (Psychiatric) problems:

All Patients

- **new or worse behavior and thought problems**
- **new or worse bipolar illness**
- **new or worse aggressive behavior or hostility**

Children and Teenagers

- **new psychotic symptoms (such as hearing voices, believing things that are not true, are suspicious) or new manic symptoms**

Tell your doctor about any mental problems you or your child have, or about a family history of suicide, bipolar illness, or depression.

Call your doctor right away if you or your child have any new or worsening mental symptoms or problems while taking Vyvanse, especially seeing or hearing things that are not real, believing things that are not real, or are suspicious.

What Is Vyvanse?

Vyvanse is a central nervous system stimulant prescription medicine. **It is used for the treatment of Attention-Deficit Hyperactivity Disorder (ADHD).** Vyvanse may help increase attention and decrease impulsiveness and hyperactivity in patients with ADHD.

Vyvanse should be used as a part of a total treatment program for ADHD that may include counseling or other therapies.

Vyvanse is a federally controlled substance (CII) because it can be abused or lead to dependence. Keep Vyvanse in a safe place to prevent misuse and abuse. Selling or giving away Vyvanse may harm others, and is against the law.

Tell your doctor if you or your child have (or have a family history of) ever abused or been dependent on alcohol, prescription medicines or street drugs.

Who should not take Vyvanse?

Vyvanse should not be taken if you or your child:

- have heart disease or hardening of the arteries
- have moderate to severe high blood pressure
- have hyperthyroidism
- have an eye problem called glaucoma
- are very anxious, tense, or agitated
- have a history of drug abuse
- are taking or have taken within the past 14 days an anti-depression medicine called a monoamine oxidase inhibitor or MAOI.
- is sensitive to, allergic to, or had a reaction to other stimulant medicines

Vyvanse has not been studied in children less than 6 years old. Vyvanse is not recommended for use in children less than 3 years old.

Vyvanse may not be right for you or your child. Before starting Vyvanse tell your or your child's doctor about all health conditions (or a family history of) including:

- heart problems, heart defects, high blood pressure
- mental problems including psychosis, mania, bipolar illness, or depression
- tics or Tourette's syndrome
- liver or kidney problems
- thyroid problems
- seizures or have had an abnormal brain wave test (EEG)

Tell your doctor if you or your child is pregnant, planning to become pregnant, or breastfeeding.

Can Vyvanse be taken with other medicines?

Tell your doctor about all of the medicines that you or your child take including prescription and nonprescription medicines, vitamins, and herbal supplements. Vyvanse and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be adjusted while taking Vyvanse.

Your doctor will decide whether Vyvanse can be taken with other medicines.

Especially tell your doctor if you or your child takes:

- anti-depression medicines including MAOIs
- anti-psychotic medicines

- lithium
- blood pressure medicines
- seizure medicines
- narcotic pain medicines

Know the medicines that you or your child takes. Keep a list of your medicines with you to show your doctor and pharmacist.

Do not start any new medicine while taking Vyvanse without talking to your doctor first.

How should Vyvanse be taken?

- **Take Vyvanse exactly as prescribed.** Vyvanse comes in 3 different strength capsules. Your doctor may adjust the dose until it is right for you or your child.
- Take Vyvanse once a day in the morning.
- Vyvanse can be taken with or without food.
- From time to time, your doctor may stop Vyvanse treatment for awhile to check ADHD symptoms.
- Your doctor may do regular checks of the blood, heart, and blood pressure while taking Vyvanse. Children should have their height and weight checked often while taking Vyvanse. Vyvanse treatment may be stopped if a problem is found during these check-ups.
- **If you or your child takes too much Vyvanse or overdoses, call your doctor or poison control center right away, or get emergency treatment.**

What are possible side effects of Vyvanse?

See **"What is the most important information I should know about Vyvanse?"** for information on reported heart and mental problems.

Other serious side effects include:
- slowing of growth (height and weight) in children
- seizures, mainly in patients with a history of seizures
- eyesight changes or blurred vision

Common side effects include:
- upper belly pain
- decreased appetite
- dizziness
- dry mouth
- irritability
- trouble sleeping
- nausea
- vomiting
- weight loss

Vyvanse may affect you or your child's ability to drive or do other dangerous activities.

Talk to your doctor if you or your child has side effects that are bothersome or do not go away.

This is not a complete list of possible side effects. Ask your doctor or pharmacist for more information

How should I store Vyvanse?

- Store Vyvanse in a safe place at room temperature, 59 to 86° F (15 to 30° C). Protect from light.
- **Keep Vyvanse and all medicines out of the reach of children.**

General information about Vyvanse

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Vyvanse for a condition for which it was not prescribed. Do not give Vyvanse to other people, even if they have the same condition. It may harm them and it is against the law.

This Medication Guide summarizes the most important information about Vyvanse. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about Vyvanse that was written for healthcare professionals. For more information about Vyvanse, please contact Shire US Inc. at 1-800-828-2088 or visit www.Vyvanse.com.

What are the ingredients in Vyvanse?

Active Ingredient: lisdexamfetamine dimesylate
Inactive Ingredients: microcrystalline cellulose, croscarmellose sodium, and magnesium stearate. The capsule shells contain gelatin, titanium dioxide, and one or more of the following: D&C Red #28, D&C Yellow #10, FC&C Blue #1 and FC&C red #40.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Tekturna®
(aliskiren)
Tablets
150 mg and 300 mg

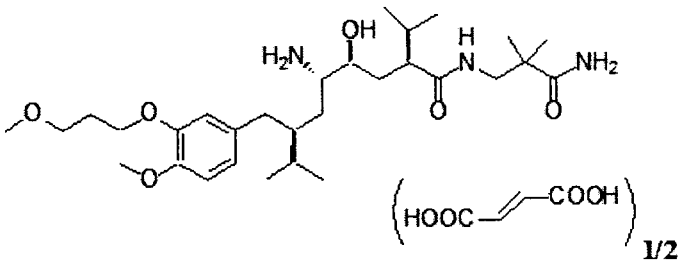
Rx only

Prescribing Information

USE IN PREGNANCY: When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. When pregnancy is detected, Tekturna should be discontinued as soon as possible. See **WARNINGS: Fetal/Neonatal Morbidity and Mortality.**

DESCRIPTION

Aliskiren, the active component of Tekturna® Tablets, is an orally active, nonpeptide, potent renin inhibitor. Aliskiren is present in Tekturna Tablets as its hemifumarate salt. Aliskiren hemifumarate is chemically described as (2S,4S,5S,7S)-N-(2-Carbamoyl-2-methylpropyl)-5-amino-4-hydroxy-2,7-diisopropyl-8-[4-methoxy-3-(3-methoxypropoxy)phenyl]-octanamide hemifumarate and its structural formula is



Molecular formula: $C_{30}H_{53}N_3O_6 \cdot 0.5\ C_4H_4O_4$

Aliskiren hemifumarate is a white to slightly yellowish crystalline powder with a molecular weight of 609.8 (free base- 551.8). It is soluble in phosphate buffer, n-Octanol, and highly soluble in water. Tekturna is available for oral administration as film-coated tablets containing 150 mg, and 300 mg of aliskiren base and the following inactive ingredients: colloidal silicon dioxide, crospovidone, hypromellose, iron oxide colorants, magnesium stearate, microcrystalline cellulose, polyethylene glycol, povidone, talc, and titanium dioxide.

CLINICAL PHARMACOLOGY

Mechanism of Action
Renin is secreted by the kidney in response to decreases in blood volume and renal perfusion. Renin cleaves angiotensinogen to form the inactive decapeptide angiotensin I (Ang I). Ang I is converted to

the active octapeptide angiotensin II (Ang II) by angiotensin-converting enzyme (ACE) and non-ACE pathways. Ang II is a powerful vasoconstrictor and leads to the release of catecholamines from the adrenal medulla and prejunctional nerve endings. It also promotes aldosterone secretion and sodium reabsorption. Together, these effects increase blood pressure. Ang II also inhibits renin release, thus providing a negative feedback to the system. This cycle, from renin through angiotensin to aldosterone and its associated negative feedback loop, is known as the renin-angiotensin-aldosterone system (RAAS). Aliskiren is a direct renin inhibitor, decreasing plasma renin activity (PRA) and inhibiting the conversion of angiotensinogen to Ang I. Whether aliskiren affects other RAAS components, e.g., ACE or non-ACE pathways, is not known.

All agents that inhibit the RAAS, including renin inhibitors, suppress the negative feedback loop, leading to a compensatory rise in plasma renin concentration. When this rise occurs during treatment with ACE inhibitors and ARBs, the result is increased levels of PRA. During treatment with aliskiren, however, the effect of increased renin levels is blocked, so that PRA, Ang I and Ang II are all reduced, whether aliskiren is used as monotherapy or in combination with other antihypertensive agents. PRA reductions in clinical trials ranged from approximately 50%-80%, were not dose-related and did not correlate with blood pressure reductions. The clinical implications of the differences in effect on PRA are not known.

Pharmacokinetics
Aliskiren is a poorly absorbed (bioavailability about 2.5%) drug with an approximate accumulation half life of 24 hours. Steady-state blood levels are reached in about 7-8 days.

Absorption and Distribution
Following oral administration, peak plasma concentrations of aliskiren are reached within 1 to 3 hours. When taken with a high fat meal, mean AUC and C_{max} of aliskiren are decreased by 71% and 85%, respectively. In the clinical trials of aliskiren, it was administered without requiring a fixed relation of administration to meals.

Metabolism and Elimination
About one-fourth of the absorbed dose appears in the urine as parent drug. How much of the absorbed dose is metabolized is unknown. Based on the in vitro studies, the major enzyme responsible for aliskiren metabolism appears to be CYP 3A4.

Special Populations

Pediatric
The pharmacokinetics of aliskiren have not been investigated in patients <18 years of age.

Geriatric
The pharmacokinetics of aliskiren were studied in the elderly (≥65 years). Exposure (measured by AUC) is increased in elderly patients. Adjustment of the starting dose is not required in these patients (see DOSAGE AND ADMINISTRATION).

Race
The pharmacokinetic differences between Blacks, Caucasians and the Japanese are minimal.

Renal Insufficiency
The pharmacokinetics of aliskiren were evaluated in patients with varying degrees of renal insufficiency. Rate and extent of exposure (AUC and C_{max}) of aliskiren in subjects with renal impairment did not show a consistent correlation with the severity of renal impairment. Adjustment of the starting dose is not required in these patients (see DOSAGE AND ADMINISTRATION).

Hepatic Insufficiency
The pharmacokinetics of aliskiren were not significantly affected in patients with mild-to- severe liver disease. Consequently, adjustment of the starting dose is not required in these patients (see DOSAGE AND ADMINISTRATION).

Cardiac Electrophysiology
Aliskiren's effects on ECG intervals were studied in a randomized, double-blind, placebo and active-controlled (moxifloxacin), 7-day repeat dosing study with Holter-monitoring and 12-lead ECGs throughout the interdosing interval. No effect of aliskiren on QT interval was seen.

Drug Interactions

Effects of Other Drugs on Aliskiren
Based on in-vitro studies, aliskiren is metabolized by CYP 3A4.
Co-administration of lovastatin, atenolol, warfarin, furosemide, digoxin, celecoxib, hydrochlorothiazide, ramapril, valsartan, metformin and amlodipine did not result in clinically significant increases in aliskiren exposure.
Co-administration of irbesartan reduced aliskiren C_{max} up to 50% after multiple dosing.
Co-administration of atorvastatin resulted in about a 50% increase in aliskiren C_{max} and AUC after multiple dosing.

Ketoconazole
Co-administration of 200 mg twice-daily ketoconazole with aliskiren resulted in an approximate 80% increase in plasma levels of aliskiren. A 400 mg once-daily dose was not studied but would be expected to increase aliskiren blood levels further.

Effects of Aliskiren on Other Drugs
Aliskiren does not inhibit the CYP450 isoenzymes (CYP1A2, 2C8, 2C9, 2C19, 2D6, 2E1, and CYP 3A) or induce CYP 3A4.
Co-administration of aliskiren did not significantly affect the pharmacokinetics of lovastatin, digoxin, valsartan, amlodipine, metformin, celecoxib, atenolol, atorvastatin, ramipril or hydrochlorothiazide.

Warfarin
The effects of aliskiren on warfarin pharmacokinetics have not been evaluated in a well-controlled clinical trial.

Furosemide
When aliskiren was co-administered with furosemide, the AUC and C_{max} of furosemide were reduced by about 30% and 50%, respectively.

CLINICAL TRIALS

Aliskiren Monotherapy

The antihypertensive effects of Tekturna® (aliskiren) have been demonstrated in six randomized, double-blind, placebo-controlled 8-week clinical trials in patients with mild-to-moderate hypertension. The placebo response and placebo-subtracted changes from baseline in seated trough cuff blood pressure are shown in Table 1.

Table 1: Reductions in Seated Trough Cuff Blood Pressure in the Placebo-Controlled Studies

		Aliskiren daily dose, mg			
Study	Placebo	75	150	300	600
	Mean change	Placebo-subtracted	Placebo-subtracted	Placebo-subtracted	Placebo-subtracted
1	2.9/3.3	5.7/4*	5.9/4.5*	11.2/7.5*	--
2	5.3/6.3	--	6.1/2.9*	10.5/5.4*	10.4/5.2*
3	10/8.6	2.2/1.7	2.1/1.7	5.1/3.7*	--
4	7.5/6.9	1.9/1.8	4.8/2*	8.3/3.3*	--
5	3.8/4.9	--	9.3/5.4*	10.9/6.2*	12.1/7.6*
6	4.6/4.1	--	--	8.4/4.9†	--

*p<0.05 vs. placebo by ANCOVA with Dunnett's procedure for multiple comparisons
†p<0.05 vs. placebo by ANCOVA for the pairwise comparison.

The studies included approximately 2730 patients given doses of 75-600 mg of aliskiren and 1231 patients given placebo. As shown in Table 1, there is some increase in response with administered dose in all studies, with reasonable effects seen at 150-300 mg, and no clear further increase at 600 mg. A substantial proportion (85%-90%) of the blood pressure lowering effect was observed within 2 weeks of treatment. Studies with ambulatory blood pressure monitoring showed reasonable control throughout the interdosing interval; the ratios of mean daytime to mean nighttime ambulatory BP ranged from 0.6 to 0.9.

Patients in the placebo-controlled trials continued open-label aliskiren for up to one year. A persistent blood pressure lowering effect was demonstrated by a randomized withdrawal study (patients randomized to continued drug or placebo), which showed a statistically significant difference between patients kept on aliskiren and those randomized to placebo. With cessation of treatment, blood pressure gradually returned toward baseline levels over a period of several weeks. There was no evidence of rebound hypertension after abrupt cessation of therapy.

Aliskiren lowered blood pressure in all demographic subgroups, although Black patients tended to have smaller reductions than Caucasians and Asians, as has been seen with ACE inhibitors and ARBs.

Aliskiren in Combination with Other Antihypertensives

Aliskiren 75, 150, and 300 mg and hydrochlorothiazide 6.25, 12.5, and 25 mg were studied alone and in combination in an 8-week, 2,776-patient, randomized, double-blind, placebo-controlled, parallel-group, 15-arm factorial study. Blood pressure reductions with the combinations were greater than the reductions with the monotherapies as shown in Table 2.

Diuretics

Table 2: Placebo-Subtracted Reductions in Seated Trough Cuff Blood Pressure in Combination with Hydrochlorothiazide

		Hydrochlorothiazide, mg			
Aliskiren, mg	Placebo mean change	0	6.25	12.5	25
		Placebo-subtracted	Placebo-subtracted	Placebo-subtracted	Placebo-subtracted
0	7.5/6.9	–	3.5/2.1	6.4/3.2	6.8/2.4
75	–	1.9/1.8	6.8/3.8	8.2/4.2	9.8/4.5
150	–	4.8/2	7.8/3.4	10.1/5	12/5.7
300	–	8.3/3.3	–	12.3/7	13.7/7.3

Valsartan
Aliskiren 150 and 300 mg and valsartan 160 and 320 mg were studied alone and in combination in an 8-week, 1,797-patient, randomized, double-blind, placebo-controlled, parallel-group, 4-arm, dose-escalation study. The dosages of aliskiren and valsartan were started at 150 and 160 mg, respectively, and increased at four weeks to 300 mg and 320 mg, respectively. Seated trough cuff blood pressure was measured at baseline, 4, and 8 weeks. Blood pressure reductions with the combinations were greater than the reductions with the monotherapies as shown in Table 3.

Table 3: Placebo-Subtracted Reductions in Seated Trough Cuff Blood Pressure in Combination with Valsartan

Aliskiren mg	Placebo mean change	Valsartan, mg		
		0	160	320
0	4.6/4.1*	–	5.6/3.9	8.2/5.6
150	–	5.4/2.7	10.0/5.7	–
300	–	8.4/4.9	–	12.6/8.1

* The placebo change is 5.2/4.8 for week 4 endpoint which was used for the dose groups containing Aliskiren 150 mg or Valsartan 160 mg.

ACE inhibitors and Amlodipine
Aliskiren has not been studied when added to maximal doses of ACE inhibitors to determine whether aliskiren produces additional blood pressure reduction with a maximal dose of an ACE inhibitor. Aliskiren 150 mg provided additional blood pressure reduction when co-administered with amlodipine 5 mg in one study, but the combination was not statistically significantly better than amlodipine 10 mg.

INDICATIONS AND USAGE

Tekturna® (aliskiren) is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents. Use with maximal doses of ACE inhibitors has not been adequately studied.

WARNINGS

Fetal/Neonatal Morbidity and Mortality
Drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women. Several dozen cases have been reported in the world literature in patients who were taking angiotensin-converting enzyme inhibitors. When pregnancy is detected, Tekturna® (aliskiren) should be discontinued as soon as possible.