



**Therapeutic Class Review<sup>SM</sup>**  
**Cardiology – Aliskiren (Tekturna<sup>®</sup>)**  
**July 2007**

**New Product for Review:**  
 aliskiren (Tekturna<sup>®</sup>) [Novartis]

**Dossier Provided by Manufacturer:** Yes  
**Dossier Evaluation:** 2

- 1- Dossier missing significant clinical trial(s).
- 2- Mfg provided all relevant trials; Missing pharmacoeconomic model.
- 3- Mfg provided all relevant trials and information.

**Available Therapeutic Alternatives:**

Preferred/Formulary	Non-Preferred/Non-Formulary
benazepril (Lotensin <sup>®</sup> ) [generics]	aliskiren (Tekturna <sup>®</sup> ) [Novartis]
captopril (Capoten <sup>®</sup> ) [generics]	candesartan (Atacand <sup>®</sup> ) [AstraZeneca]
enalapril (Vasotec <sup>®</sup> ) [generics]	eprosartan (Teveten <sup>®</sup> ) [Kos]
fosinopril (Monopril <sup>®</sup> ) [generics]	irbesartan (Avapro <sup>®</sup> ) [BMS]
lisinopril (Zestril <sup>®</sup> ) [generics]	losartan (Cozaar <sup>®</sup> ) [Merck]
moexipril (Univasc <sup>®</sup> ) [generics]	perindopril (Aceon <sup>®</sup> ) [Solvay]
olmesartan (Benicar <sup>®</sup> ) [Daiichi Sankyo]	ramipril (Altace <sup>®</sup> ) [Monarch]
quinapril (Accupril <sup>®</sup> ) [generics]	valsartan (Diovan <sup>®</sup> ) [Novartis]
telmisartan (Micardis <sup>®</sup> ) [Boehringer Ingelheim]	
trandolapril (Mavik <sup>®</sup> ) [generics]	

**Executive Summary**

- High blood pressure is associated with an increased risk of cardiovascular and cerebrovascular events.
  - The higher the blood pressure, the greater the chance of heart attack, heart failure, stroke, and kidney disease.
  - The risk is consistent and independent of other risk factors.
- The ultimate goal of antihypertensive therapy is to reduce cardiovascular and renal morbidity and mortality.
- National and International Guidelines recommend a diuretic as initial treatment for hypertension for the majority of patients.
- Most patients will require two or more agents to achieve optimal control of their blood pressure.
- Aliskiren (Tekturna), like angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), lowers blood pressure via its action on the renin-angiotensin-aldosterone system (RAAS).

- The manufacturer promotes aliskiren (Tekturna) as having potential advantages over ACEIs and ARBs due to its unique (first in class), direct inhibition of renin; however, there is no evidence that supports any clinical significance of this in clinical practice.
- There are many preferred/formulary options from many different classes available for treatment of hypertension. These options include diuretics, beta-blockers, calcium channel blockers (CCBs), alpha-blockers, aldosterone antagonists, ACEIs, ARBs, and direct vasodilators.
- Generic options (including diuretics, CCBs, ACEIs, and beta-blockers) offer the best value for treatment of hypertension because they have proven benefit in reducing cardiovascular death, stroke, and/or progression of renal failure.

## Evidence

- The efficacy and safety of aliskiren (Tekturna) are based on trials of short duration (approximately 8 weeks in length) studying diastolic blood pressure (DBP) lowering as a primary endpoint.
- There is no evidence that aliskiren (Tekturna) is better at lowering blood pressure than:
  - Optimal doses of other antihypertensive agents.
  - ACEIs or ARBs.
- There is no direct evidence that aliskiren (Tekturna) decreases the risk of cardiovascular morbidity and mortality, stroke, or progression of renal failure.
- There is no evidence that combining aliskiren (Tekturna) with an ACEI or ARB is superior to maximizing the dose of the ACEI or ARB.
- Aliskiren (Tekturna) has not demonstrated improved safety or tolerability over ACEIs or ARBs.

## *Considerations in Subpopulations:*

- **Pediatrics:** Safety and effectiveness of aliskiren in pediatric patients have not been established.
- **Geriatrics:** Elderly patients (> 65 years) respond to lower doses than younger patients.<sup>[1]</sup> Some adverse effects (e.g., diarrhea) occurred at lower doses in elderly patients.<sup>[2]</sup>
- **Gender:** No difference in efficacy is noted between women and men in the package labeling. At equal doses, higher rates of diarrhea were seen in women than in men.<sup>[2]</sup>
- **Race, ethnicity:** Black patients show a reduced antihypertensive response to aliskiren (Tekturna) than white patients, and Asian patients respond to lower doses of aliskiren (Tekturna) than white patients.<sup>[1]</sup>

## Conclusion

Aliskiren (Tekturna) is non-preferred/non-formulary because:

- There are many preferred/formulary antihypertensive options available (many of them generics) that provide an excellent value to our members.
- There is no evidence of additional benefit over current preferred/formulary options.

## Products

Drug Products	FDA approval <sup>a</sup>	Patent Expiration(s) <sup>c</sup>	FDA approved indications	Usual Dose/Route	Cost <sup>b</sup>	Potential Off-label Uses <sup>d</sup>
Aliskiren (Tekturna <sup>®</sup> ) <sup>[2]</sup>	3/2007	3/2012	<ul style="list-style-type: none"> <li>Hypertension</li> </ul>	150 mg to 300 mg once daily	\$73 to \$93	
benazepril <sup>[3]</sup> (generics)	6/1991	expired	<ul style="list-style-type: none"> <li>Hypertension</li> </ul>	20 to 40 mg once daily Max: 80 mg qd	\$6 to \$7	Angina; congestive heart failure; Diabetic nephropathy; non-diabetic kidney dx; myocardial infarction
enalapril <sup>[4]</sup> (generics)	12/1985	expired	<ul style="list-style-type: none"> <li>Hypertension</li> <li>Heart Failure</li> <li>Asymptomatic left ventricular dysfunction</li> </ul>	10 mg to 40 mg divided once or twice per day (hypertension)	\$2 to \$3	Diabetic nephropathy; non-diabetic kidney dx; malignant hypertension; migraine px; Raynaud's; atherosclerosis
fosinopril <sup>[5]</sup> (generics)	5/1991	expired	<ul style="list-style-type: none"> <li>Hypertension</li> <li>Heart Failure</li> </ul>	20 mg to 40 mg once daily Max: 80 mg qd (hypertension)	\$6 to \$25 20mg: \$0.85 40mg: \$0.20	Diabetic nephropathy; non-diabetic kidney dx; myocardial infarction
lisinopril <sup>[6]</sup> (generics)	12/1987	expired	<ul style="list-style-type: none"> <li>Hypertension</li> <li>Heart Failure</li> <li>Acute myocardial infarction</li> </ul>	20 mg to 40 mg once daily	\$3 to \$9	Diabetic nephropathy; non-diabetic kidney dx; malignant hypertension; migraine px
olmesartan (Benicar <sup>®</sup> ) <sup>[7]</sup>	4/2002	4/2016 11/2021	<ul style="list-style-type: none"> <li>Hypertension</li> </ul>	20 mg to 40 mg once daily	\$56 to \$65	
telmisartan (Micardis <sup>®</sup> ) <sup>[8]</sup>	11/1998	1/2014 1/2020	<ul style="list-style-type: none"> <li>Hypertension</li> </ul>	40 mg to 80 mg once daily	\$61 o \$65	Congestive heart failure; left ventricular hypertrophy

<sup>a</sup> Date applies to approval date for the original brand name medication where there are now generics available.

<sup>b</sup> Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of May 2007 for 1 month of therapy.

<sup>c</sup> Based on patents listed in Orange Book as of 05/14/07.

<sup>d</sup> As listed in © 1974 - 2007 Thomson MICROMEDEX database or as referenced.

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