

Indiana Medicaid Therapeutics Committee Therapeutic Class Review Summary

Therapeutic Class:

Angiotensin II Receptor Blockers in combination with Calcium Channel Blockers

Overview:

Angiotensin Receptor Blockers (ARBs) are a class of agents used alone, or in combination, in the management of hypertension. Angiotensin II, a potent vasoconstrictor, is formed from angiotensin I in a reaction catalyzed by angiotensin converting enzyme (ACE). It is the primary vasoactive hormone of the renin-angiotensin system with effects that include vasoconstriction, stimulation of aldosterone secretion, cardiac stimulation, and renal reabsorption of sodium. ARBs such as olmesartan and valsartan, block the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT₁ receptors in many tissues including vascular smooth muscle and the adrenal gland. According to The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VII Guidelines), ARBs are considered an initial drug therapy option for management of Stage I and Stage II hypertension. In addition, ARBs are recommended as initial drug therapy for the treatment of pre-hypertension and hypertension in patients with specific compelling indications such as diabetes, heart failure, and chronic kidney disease.

The contractile processes of cardiac muscle and vascular smooth muscle depend upon the movement of extracellular calcium ions into the cells through specific ion channels. Calcium channel blockers (CCBs) inhibit the transmembrane influx of calcium ions into the vascular smooth muscle and the cardiac muscle, resulting in increased oxygen delivery to myocardial tissue, smooth muscle relaxation, vasodilation, decreased total peripheral resistance, and decreased systemic blood pressure. Serum calcium levels are not affected by CCBs. There are two types of CCBs: dihydropyridines (DHP) and non-dihydropyridines (NDHP). In addition to peripheral artery dilation, NDHP CCBs, which include diltiazem and verapamil, dilate the main coronary arteries and slow AV nodal conduction, making these agents effective in the treatment of angina and supraventricular arrhythmias. DHP CCBs, which include amlodipine, felodipine, isradipine, nicardipine, nifedipine, and nisoldipine, produce a more potent peripheral vasodilating effect. Amlodipine acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in blood pressure. According to The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VII Guidelines), CCBs are considered an initial drug therapy option for management of Stage I and stage II hypertension. CCBs are also recommended as initial drug therapy for treatment of pre-hypertension and hypertension in specific compelling indications such as diabetes and high coronary disease risk.

Currently there are two fixed-dose CCB/ARB combination products available in the U.S. market: AzorTM and Exforge[®]. Both are approved by the FDA for the treatment of hypertension; however, only Exforge[®] has an indication for initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals.

Generic Name	Brand Name	Manufacturer	Generic Available
Amlodipine/Olmesartan Medoxomil	Azor TM	Daiichi Sankyo	No
Amlodipine/Valsartan	Exforge [®]	Novartis	No

Summary:

Considering the benefit for treatment-resistant patients and the reduced incidence of peripheral edema, either AzorTM or Exforge[®] should be considered for inclusion on the preferred drug list. These combination products have been proven both safe and effective. Moreover, combination products have been shown to produce greater BP reductions when compared to monotherapy. Currently, there are no head to head comparative studies evaluating these combination agents. PDL inclusion should be based on available clinical trial information demonstrating the safety and efficacy of these combination products as well as safety and efficacy of the individual components.