Indiana Medicaid Therapeutics Committee
Therapeutic Class Review Summary

Therapeutic Class:
Angiotensin Converting Enzyme Inhibitors in combination with Diuretics

Overview:
Angiotensin Converting Enzyme (ACE) inhibitors are a class of medications used to manage hypertension. ACE inhibitors compete with angiotensin I for its binding site on the angiotensin-converting enzyme. As a result, ACE inhibitors block the conversion of angiotensin I to angiotensin II; angiotensin II is a potent vasoconstrictor. When angiotensin II is blocked, there is an increase in plasma renin activity. Decreases in plasma angiotensin II levels also result in a reduction of aldosterone secretion, with a subsequent decrease in sodium and water retention. ACE inhibitors are effective in reducing blood pressure. Since these agents reduce glomerular blood pressure, these agents also have shown some renoprotective effects. ACE inhibitors can also counteract the hypokalemia caused by thiazide diuretics.

Hydrochlorothiazide (HCTZ) is a thiazide diuretic. The mechanism of the antihypertensive effect of thiazides is increasing the excretion of water by inhibiting the reabsorption of sodium and chloride ions at the distal renal tubule; thiazide diuretics also reduce peripheral vascular resistance by an unknown mechanism. Thiazide diuretics may induce hypokalemia as a result of increases in plasma renin activity and aldosterone secretion. Thiazides do not usually exert a pharmacologic effect on normal blood pressure.

The fixed-dose combinations of ACE inhibitors and diuretics are approved by the FDA for the treatment of hypertension and seem to have an additive affect on blood pressure. However, they are not indicated as initial therapy. There are data supporting use of these fixed-dose combinations in treatment resistant patients. Currently, there are seven ACE inhibitor/diuretic fixed-dose combination products available in the U.S. market, and all products are available as generics. Clinical trial data comparing safety and efficacy of these combinations with one another is very limited.

Generic Name	Trade Name	Dose	Manufacturer	Generic
Quinapril / HCTZ	Accuretic®	10/12.5, 20/12.5, 20/25 mg	Parke-Davis, various	Y
Benazepril / HCTZ	Lotensin HCT®	5/6.25, 10/12.5, 20/12.5, 20/25 mg	Novartis	Y
Fosinopril / HCTZ	Monopril HCT®	10/12.5, 20/12.5 mg	Bristol-Myers Squibb	Y
Lisinopril / HCTZ	Prinzide®	10/12.5, 20/12.5, 20/25 mg	Merck	Y
	Zestoretic®	10/12.5, 20/12.5, 20/25 mg	Astra-Zeneca	Y
Moexipril / HCTZ	Uniretic®	7.5/12.5, 15/12.5, 15/25 mg	Schwarz	Y
Enalapril / HCTZ	Vaseretic®	5/12.5, 10/25 mg	Biovail	Y
Captopril / HCTZ	Capozide®	25/15, 25/25, 50/15, 50/25mg	Par	Y

Summary:
Given the benefit for treatment resistant patients as well as decreased concern about potassium levels with the individual agents, the recommendation is to consider adding at least two combination products to the preferred drug list. There are studies to support the safety and efficacy of generically available lisinopril/HCTZ. Many of these products are available in various strengths. The effectiveness of these fixed-dose combination products is additive versus individual agents alone, and the medications have similar side effect profiles.