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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, plasma renin activity is increased. 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, they also have shown some renoprotective effect. Furthermore, ACE inhibitors can 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 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, seven ACE inhibitor/diuretic fixed-dose combination products are available in the U.S. market. All products are offered as generics. Clinical trial data comparing safety and efficacy of these combinations with one another are very limited.



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Generic Name	Trade Name	Manufacturer	Generic
Quinapril / HCTZ	Accuretic [®] , various	Parke-Davis	Y
Benazepril / HCTZ	Lotensin HCT [®]	Novartis	Y
Fosinopril / HCTZ	Monopril HCT [®]	Bristol-Myers Squibb	Y
Lisinopril / HCTZ	Prinzide [®]	Merck	Y
	Zestoretic [®]	Astra-Zeneca	Y
Moexipril / HCTZ	Uniretic [®]	Schwarz	Y
Enalapril / HCTZ	Vaseretic [®]	Biovail	Y
Captopril / HCTZ	Capozide [®]	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. Studies supporting the safety and efficacy of generically available lisinopril/HCTZ do exist. 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.