

**Indiana Medicaid Therapeutics Committee**  
**Therapeutic Class Review Summary**

**Therapeutic Class:**

Angiotensin Receptor Blockers in combination with a Diuretic

**Overview:**

Angiotensin receptor blockers (ARBs) in combination with hydrochlorothiazide were first approved in 1998. The mechanism of action for ARBs is via selective blockade of the binding of angiotensin II to the AT<sub>1</sub> receptor. The antihypertensive mechanism of action of hydrochlorothiazide is increased 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.

There are currently seven ARB/HCTZ combinations available on the U.S. market indicated for the use of hypertension. Hyzaar<sup>®</sup> has an additional indication for initial use in appropriate patients with severe hypertension. Additionally, Avalide<sup>®</sup> and Diovan HCT<sup>®</sup> are approved for initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals. Hyzaar<sup>®</sup> is also indicated to reduce the risk of stroke in patients with hypertension and left ventricular hypertrophy, but there is evidence that this benefit does not apply to African Americans. At this time, none of the agents are available generically. ARB/HCTZ combinations are generally well tolerated with few adverse reactions. Headache, dizziness, and upper respiratory tract infections are the most commonly reported adverse reactions. Increases in serum uric acid levels have been reported with concurrent ARB and HCTZ therapy.

All ARB/HCTZ combinations have data supporting their efficacy in lowering blood pressure. Combination therapy is especially useful when monotherapy is ineffective. There are few outcome studies measuring mortality and morbidity.

Generic Name	Brand Name	Manufacturer	Generic Available
Candesartan/HCTZ	Atacand HCT <sup>®</sup>	AstraZeneca	N
Eprosartan/HCTZ	Teveten HCT <sup>®</sup>	Solvay	N
Irbesartan/HCTZ	Avalide <sup>®</sup>	Bristol-Myers Squibb	N
Losartan/HCTZ	Hyzaar <sup>®</sup>	Merck & Co., Inc.	N
Olmesartan/HCTZ	Benicar HCT <sup>®</sup>	Sankyo	N
Telmisartan/HCTZ	Micardis HCT <sup>®</sup>	Boehringer Ingelheim	N
Valsartan/HCTZ	Diovan HCT <sup>®</sup>	Novartis	N

**Summary:**

Given the differences in patient response, at least two agents should be added to the preferred drug list. Losartan/HCTZ and valsartan/HCTZ have the most clinical data supporting their effectiveness in treating hypertension. For patients refractory to the two

previously mentioned agents, telmisartan/HCTZ appears to have the highest response rate. Thus, its availability on the PDL may be necessary. Losartan/HCTZ has an additional indication for initial use in appropriate patients with severe hypertension and an additional indication to reduce the risk of stroke in patients with hypertension and left ventricular hypertrophy (not applicable in African Americans). Irbesartan/HCTZ and valsartan/HCTZ are also approved for initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals. Future clinical trials detailing the long-term outcomes associated with these medications will help to provide guidance on PDL inclusion.