

Indiana Medicaid Therapeutics Committee Therapeutic Class Review Summary

Therapeutic Class:

Direct Renin Inhibitor-Diuretic Combination Product

Overview:

Aliskiren HCT (Tekturna HCT) is a combination agent indicated for the treatment of hypertension as add-on therapy or as replacement therapy for titrated aliskiren and HCTZ. Like angiotensin converting enzyme inhibitors and angiotensin receptor blockers, aliskiren exerts its activity on the renin-angiotensin system. Aliskiren is a potent, direct inhibitor of renin. Renin facilitates the conversion of angiotensinogen to angiotensin I, which is subsequently cleaved by angiotensin-converting enzyme to form angiotensin II, a potent vasoconstrictor. Therefore, aliskiren prevents the ultimate formation of angiotensin II, thus causing a reduction in blood pressure. Whether aliskiren affects any other step in the cascade is unknown at this time. Hydrochlorothiazide (HCTZ) is a thiazide diuretic that affects renal tubular mechanisms of electrolyte reabsorption and directly increases the excretion of sodium and chloride in approximately equivalent amounts. Hydrochlorothiazide also indirectly reduces plasma volume and subsequently increases plasma renin activity, increases aldosterone secretion, increases urinary potassium loss, and decreases serum potassium.

Aliskiren HCT is available as 150/12.5mg, 150/25mg, 300/12.5mg, and 300/25mg tablets for once-daily administration. Antihypertensive effects are usually seen within one week with maximal effects seen at around four weeks. Aliskiren may be administered without regard to food; however, aliskiren should be taken consistently, since high-fat meals can result in a significant decrease in absorption. Common adverse effects associated with the use of aliskiren HCT include diarrhea, dizziness, and influenza.

As with other medications that exert their action on the renin-angiotensin-aldosterone system, aliskiren HCT has a black box warning regarding its use in pregnancy. Aliskiren can lead to injury and possibly death of the developing fetus when administered during pregnancy. Therefore, this medication should not be given to pregnant women.

Generic Name	Brand Name	Manufacturer
Aliskiren HCT	Tekturna HCT	Novartis Pharmaceuticals

Summary:

Aliskiren/HCTZ, a novel antihypertensive combination agent, has produced blood pressure reductions superior to aliskiren or HCTZ monotherapy. When compared to other combination regimens, aliskiren/HCTZ provided comparable efficacy in one of the studies but provided significantly greater BP reductions than ramipril-based therapy in another study. Whether aliskiren/HCTZ has an effect on outcome measures (such as heart attack, stroke, or nephropathy) is currently unknown. While aliskiren/HCTZ was relatively well tolerated in clinical trials, the most common adverse effects associated with therapy are dizziness, diarrhea, and influenza.