

Indiana Medicaid Therapeutics Committee Therapeutic Class Review Summary

Therapeutic Class:

Angiotensin Receptor Antagonist-Calcium Channel Blocker-Thiazide Combination

Overview:

Amlodipine/ Valsartan/Hydrochlorothiazide (Exforge HCT[®]) is a combination agent indicated for the treatment of hypertension as add-on/switch therapy or as replacement therapy for titrated amlodipine, valsartan, and hydrochlorothiazide. The active ingredients in Exforge HCT[®] target three separate mechanisms involved in blood pressure regulation. Amlodipine is a dihydropyridine calcium channel blocker that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle and blocks the contractile effects of calcium in these tissues. Valsartan selectively blocks the binding of angiotensin II to the AT1 receptors in cardiac, vascular smooth muscle, adrenal and renal cells and therefore, prevents the vasoconstriction and sodium retaining effects of angiotensin II. 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, aldosterone secretion, and urinary potassium loss while decreasing serum potassium.

Exforge HCT[®] is available as amlodipine/valsartan/HCTZ in 5/160/12.5mg, 10/160/12.5mg, 5/160/25mg, 10/160/25mg, and 10/320/25mg tablets for once-daily administration with or without food. The full antihypertensive effects are achieved two weeks after being on the maximal dose of 10/320/25mg. Common adverse events associated with the use of Exforge HCT[®] include dizziness, edema, headache, dyspepsia, and lab abnormalities.

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

Generic Name	Brand Name	Manufacturer
Amlodipine; Valsartan; Hydrochlorothiazide	Exforge HCT [®]	Novartis Pharmaceuticals

Summary:

Amlodipine/Valsartan/Hydrochlorothiazide (Exforge HCT[®]), a triple antihypertensive combination product, has produced blood pressure reductions superior to the individual agents used in dual therapy combinations. At this time, it is unknown whether Exforge HCT[®] has an effect on outcome measures such as heart attack, stroke, or nephropathy. While it was relatively well tolerated in a clinical trial, the most common adverse events associated with therapy are dizziness, edema, headache, dyspepsia, and lab abnormalities.