

## NEW DRUG UPDATE

<b>Drug Name:</b>	aliskiren / amlodipine / hydrochlorothiazide (HCTZ)
<b>Trade Name (Manufacturer):</b>	Amturnide™ (Novartis)
<b>Form:</b>	tablets
<b>Strength:</b>	150/5/12.5, 300/5/12.5, 300/5/25, 300/10/12.5, and 300/10/25 mg
<b>FDA Approval:</b>	December 21, 2010
<b>Market Availability:</b>	Now available
<b>FDA Approval Classification:</b>	Standard review
<b>Classification:</b>	Specific Therapeutic Class (HIC3): Renin Inhib, Direct/Calc. Chnnel Blkr/Thiazide Cb (A4Z)

**Indication:**<sup>1</sup> A combination of a direct renin inhibitor, non-dihydropyridine calcium channel blocker, and thiazide diuretic, aliskiren/amlodipine/HCTZ (Amturnide) is indicated for the treatment of hypertension. The combination is not indicated for initial therapy, but for patients not adequately controlled with products from two of the three component drug classes.

**Contraindications/Warnings:** Aliskiren/amlodipine/HCTZ is contraindicated in patients with anuria or hypersensitivity to sulfonamide-derived drugs.

Fetal and neonatal exposure to this combination product should be avoided. Patients who experience head and neck angioedema should discontinue therapy. Volume- or salt-depleted patients need to have imbalances corrected prior to initiating therapy. Patients may experience increased angina or myocardial infarction due to dose changes in the amlodipine component. This product should be avoided in patients with severe renal impairment and titrated gradually in those with hepatic impairment.

### **Drug Interactions:**

aliskiren: Because aliskiren is metabolized by CYP450 3A4 enzymes, concomitant use with cyclosporine or itraconazole is not recommended. Aliskiren does not affect the CYP450 enzyme system.

amlodipine: There are no significant drug interactions with this component.

HCTZ: Interactions may occur with concurrent administration of alcohol, barbiturates, or opioid analgesics (orthostatic hypotension); bile acid resins (impaired HCTZ absorption); corticosteroids (electrolyte depletion); lithium (lithium toxicity); or NSAIDs (reduced HCTZ efficacy).

**Common Adverse Effects:** In a trial that administered the fixed combination of aliskiren/amlodipine/HCTZ compared to aliskiren/amlodipine, aliskiren/HCTZ, and amlodipine/HCTZ, common adverse events included the following: peripheral edema (7.1 versus 2-8 percent), dizziness (3.6 versus 1.7-3.4 percent), headache (3.6 versus 3.1-5.1 percent), and nasopharyngitis (2.6 versus 0.7-3.4 percent).

### **Special Populations:**

Pediatrics: The safety and effectiveness of aliskiren/amlodipine/HCTZ has not been established.

**Pregnancy:** D (including all trimesters during pregnancy)

**Geriatrics:** In clinical trials, no overall differences in effectiveness or safety were reported for this population.

**Renal Impairment:** Aliskiren/amlodipine/HCTZ is not recommended in patients with creatinine clearance less than 30 mL/min.

**Hepatic Impairment:** Patients with severe impairment should start amlodipine at 2.5 mg per day (this is not an option with the combination product).

**Dosages:** Aliskiren/amlodipine/HCTZ is administered once daily. Administration may occur with or without a meal, but a routine dosing pattern should be adopted. If a patient is converting from separate tablets to the combination, substitute the combination that contains the same component doses.

**Clinical Trials:** A literature search was performed using “aliskiren, amlodipine, hydrochlorothiazide” Placebo-controlled trials were included in the absence of comparative trials.

A double-blind, active-controlled study compared aliskiren/amlodipine/HCTZ to aliskiren/amlodipine, aliskiren/HCTZ, or amlodipine/HCTZ in 1,181 hypertensive patients.<sup>2</sup> The mean baseline systolic/diastolic blood pressure for all randomized patients was approximately 173/105 mmHg. After four weeks, all patients were titrated to their full target doses of aliskiren/amlodipine/HCTZ 300/10/25 mg, aliskiren/amlodipine 300/10 mg, aliskiren/HCTZ 300/25 mg, or amlodipine/HCTZ 10/25 mg. Aliskiren/amlodipine/HCTZ produced greater reductions in blood pressure than did any of the dual combination treatments (9.9/6.3 mmHg greater than with aliskiren/HCTZ, 7.2/3.6 mmHg greater than with amlodipine/HCTZ, and 6.6/2.6 mmHg greater than with aliskiren/amlodipine, all  $p < 0.001$ ). The antihypertensive effect of aliskiren/amlodipine/HCTZ was similar in patients with and without diabetes, obese and non-obese patients, in patients  $\geq 65$  years of age and  $< 65$  years of age, and in women and men.

**Other Drugs Used for Condition:** A number of therapeutic classes are used for the treatment of hypertension, including: diuretics, beta-blockers, calcium channel blockers, ACE inhibitors, angiotensin receptor blockers, and direct renin inhibitors.<sup>3</sup> Other products that combine an angiotensin modulator with a calcium channel blocker include: amlodipine/olmesartan (Azor™), amlodipine/telmisartan (Twynsta®), amlodipine/valsartan (Exforge®), amlodipine/valsartan/HCTZ (Exforge HCT®), olmesartan/amlodipine/HCTZ (Tribenzor™), amlodipine/benazepril (Lotrel®), and trandolapril/verapamil (Tarka®).

**Place in Therapy:** Aliskiren/amlodipine/HCTZ is not for initial therapy. As a fixed-dose combination product, patients should be started on the individual components and dosages titrated to achieve the desired reduction in blood pressure. The combination product should only be considered for patients on established doses of the individual components who do not achieve the desired blood pressure reduction and also demonstrate a need for combination therapy rather than continuation of individual agents.

## References

<sup>1</sup> Amturnide [package insert]. East Hanover, NJ; Novartis; December 2010.

<sup>2</sup> Amturnide [package insert]. East Hanover, NJ; Novartis; December 2010.

<sup>3</sup> Available at: [www.clinicalpharmacology.com](http://www.clinicalpharmacology.com). Accessed January 18, 2011.