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Novartis Gains FDA Approval for Amturnide™, a Triple-Combination Pill to Treat High Blood Pressure in Patients Uncontrolled on Two Medications

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- - In a clinical trial, Amturnide demonstrated significantly greater reductions in blood pressure compared to all dual combinations of its components
- - Amturnide combines the only approved direct renin inhibitor, Tekturna®, with a widely used calcium channel blocker and a diuretic to treat high blood pressure
- - Up to 85% of patients may need multiple medications to help reach blood pressure goals; difficult-to-treat patients may require three or more

EAST HANOVER, N.J., Dec. 22, 2010 /PRNewswire/ -- Today Novartis announced that the US Food and Drug Administration (FDA) approved Amturnide (aliskiren, amlodipine and hydrochlorothiazide) tablets for the treatment of high blood pressure. Amturnide combines the only approved direct renin inhibitor worldwide, Tekturna (aliskiren), with the widely used calcium channel blocker amlodipine and the diuretic hydrochlorothiazide (HCTZ).

The FDA approval was based on data from a double-blind, active controlled study, which showed that Amturnide provided significantly greater reductions in blood pressure compared to all dual combinations of its components. Amturnide is approved for patients whose blood pressure is not adequately controlled with any two of its individual components and is not indicated as initial therapy for high blood pressure. Amturnide is only the third high blood pressure treatment to combine three drugs in a single-pill.

"The FDA approval of Amturnide provides an important treatment option to help address the complex needs of high blood pressure patients," said Andre Wyss, President of Novartis Pharmaceuticals Corporation. "This approval emphasizes our commitment to cardiovascular research and to developing innovative and effective treatments for patients who have not reached their blood pressure goal."

The study involved 1,181 patients with moderately elevated blood pressure (mean systolic blood pressure [mSBP] 160-179 mmHg) or severely elevated blood pressure (mSBP >/=180 mmHg). Both patient populations achieved greater systolic and diastolic blood pressure reductions with Amturnide compared to dual combination treatment of aliskiren/amlodipine 300 mg/10 mg, aliskiren/HCTZ 300 mg/25 mg, and amlodipine/HCTZ 10 mg/25 mg.

In the overall patient population, Amturnide reduced systolic/diastolic blood pressure by an additional 9.9/6.3 mmHg compared to aliskiren/HCTZ; 7.2/3.6 mmHg compared to amlodipine/HCTZ; and 6.6/2.6 mmHg compared to aliskiren/amlodipine. In patients with severely elevated blood pressure, these reductions were greater by 16.3/8.2 mmHg, 9.6/4.8 mmHg, and 11.4/4.9 mmHg respectively.

"Some patients require three or more medications to help manage their high blood pressure, which can be challenging and inconvenient," said Alan H. Gradman, M.D., Professor of Medicine at Temple University

School of Medicine. "The approval of Amturnide provides physicians with an effective treatment option that combines the benefits of the only approved direct renin inhibitor, a calcium channel blocker and a diuretic in one pill, while offering blood pressure reductions greater than two drugs alone."

The single-pill combination Amturnide works to lower blood pressure in three ways. The Tekturna component targets the activity of the renin angiotensin aldosterone system (RAAS), an important regulator of blood pressure. Tekturna directly binds to and inhibits renin, an enzyme produced by the kidneys that starts a process that can make blood vessels narrow and lead to high blood pressure. The calcium channel blocker amlodipine lowers blood pressure by relaxing muscles in the blood vessel walls, and the diuretic hydrochlorothiazide increases the excretion of sodium chloride and water. All three complementary medicines work to relax blood vessels and reduce blood volume, therefore lowering blood pressure.

High blood pressure affects nearly 75 million adults in the United States and about one billion adults worldwide. An estimated 31% of adults being treated with antihypertensive medications are not at their blood pressure goal. Large-scale clinical trials suggest that up to 85% of patients may need multiple medicines to achieve target levels of blood pressure control, and hypertensive patients with lower blood pressure goals or with substantially elevated blood pressure may require three or more medications.

If left untreated, high blood pressure increases the risk of stroke, heart attack and heart failure. Amturnide is not approved to treat or prevent stroke, heart attack and heart failure.

Novartis and Hypertension Management

For decades Novartis has been a leader and innovator in hypertension management, offering a range of innovative therapies designed to help patients with different needs achieve their blood pressure goals. Novartis is dedicated to helping physicians and patients improve cardiovascular and metabolic health through our ongoing commitment to researching effective medicines.

Amturnide is available in five strengths as once-daily tablets containing aliskiren, amlodipine and hydrochlorothiazide: 150 mg/5 mg/12.5 mg tablets, 300 mg/5 mg/12.5 mg tablets, 300 mg/5 mg/25 mg tablets, 300 mg/10 mg/12.5 mg tablets, and 300 mg/10 mg/25 mg tablets.

About Amturnide

INDICATION

AMTURNIDE is indicated for the treatment of hypertension. AMTURNIDE is not indicated for initial therapy of hypertension.

Use AMTURNIDE for patients not adequately controlled with any two of the following: aliskiren, dihydropyridine calcium-channel blockers (DHP-CCB), and thiazide diuretics.

Switch a patient who experiences dose-limiting adverse reactions attributed to an individual component-while on any dual combination of components of AMTURNIDE- to AMTURNIDE at a lower dose of that component to achieve similar blood pressure reductions.

AMTURNIDE may be substituted for its titrated components.

Safety and efficacy of AMTURNIDE in pediatric patients have not been established.

IMPORTANT SAFETY INFORMATION

WARNING: AVOID USE IN PREGNANCY

When pregnancy is detected, discontinue AMTURNIDE as soon as possible. Drugs that act directly on the renin-angiotensin-aldosterone system can cause injury and even death to the developing fetus. [See WARNINGS and Precautions (5.1) and Use in Special Populations (8.1)].

Angioedema: Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with aliskiren and has necessitated hospitalization and intubation. This may occur at any time during treatment and has occurred in patients with and without a history of angioedema with ACE inhibitors (ACEI) or angiotensin receptor antagonists. Discontinue AMTURNIDE immediately in patients who develop angioedema and do not readminister.

Hypotension: Excessive hypotension was seen rarely (0.3%) in patients with uncomplicated hypertension treated with AMTURNIDE in a controlled trial. Volume- and/or salt-depletion should be corrected in patients prior to administration of AMTURNIDE or symptomatic hypotension may occur.

Risk of MI or Angina: Rarely, initiation or change to the dose of a calcium channel blocker has resulted in the increased frequency, duration, or severity of angina or acute myocardial infarction, particularly in patients with severe obstructive coronary artery disease.

Renal Considerations: In patients with severe renal impairment (GFR <30mL/min), loop diuretics are preferred to thiazides, so AMTURNIDE is not recommended.

No data are available on the use of AMTURNIDE in patients with unilateral or bilateral renal artery stenosis. In studies of ACEIs in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen have been reported.

Hepatic Considerations: Amlodipine is extensively metabolized by the liver. In patients with severe hepatic impairment, start amlodipine at 2.5 mg per day, a dose not available in AMTURNIDE.

Patients with Heart Failure: AMTURNIDE has not been studied in patients with heart failure.

Serum Electrolyte Abnormalities: In a short-term controlled trial, hypokalemia (serum potassium <3.5 mEq/L) was seen in 11% of patients treated with AMTURNIDE. The incidence of hyperkalemia (serum potassium >5.5 mEq/L) was 3%. No patients treated with AMTURNIDE discontinued due to increase or decrease of serum potassium. Monitor serum electrolytes to detect possible electrolyte imbalance.

Concomitant use of AMTURNIDE with potassium-sparing diuretics, potassium supplements, or other salt substitutes containing potassium may lead to increases in serum potassium.

Cyclosporine or Itraconazole: Concomitant use of AMTURNIDE with cyclosporine or itraconazole is not recommended.

Furosemide: When aliskiren was coadministered with furosemide, the AUC and Cmax of furosemide were reduced by about 30% and 50%, respectively. Patients receiving furosemide could find its effect diminished after starting aliskiren.

Important considerations due to the HCTZ component: Uptitrate HCTZ slowly in patients with renal disease, as thiazides may precipitate azotemia. Titrate HCTZ gradually in patients with hepatic impairment, as minor fluid and electrolyte balance may precipitate hepatic coma. Hypersensitivity reactions to HCTZ may occur in patients with or without a history of allergy or bronchial asthma, but are more likely in patients with such a history. Thiazide diuretics have been reported to cause exacerbation or activation of systemic lupus erythematosus. Lithium generally should not be given with thiazides.

HCTZ, a sulfonamide, can cause an idiosyncratic reaction resulting in transient myopia and angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of drug initiation. Discontinue HCTZ as rapidly as possible in these patients. Risk factors for developing acute angle-closure glaucoma may include a history of sulfonamide or penicillin allergy.

Common AEs: The most common adverse events in a short-term controlled trial that occurred in at least 2% of patients treated with AMTURNIDE were peripheral edema (7.1%), dizziness (3.6%), headache (3.6%), and nasopharyngitis (2.6%).

For full prescribing information, log onto www.pharma.us.novartis.com or contact Christine Cascio at 1-862-778-8026 or christine.cascio@novartis.com.

About Tekturna

TEKTURNA is a prescription medicine for adults used to treat high blood pressure. TEKTURNA may be used alone or in combination with other medicines to lower high blood pressure. TEKTURNA has not been adequately studied in combination with the maximum doses of a class of medicines called ACE inhibitors.

IMPORTANT SAFETY INFORMATION

IMPORTANT WARNING: TEKTURNA may harm an unborn baby, causing injury and even death. If you get pregnant, stop taking TEKTURNA and call your doctor right away. If you plan to become pregnant, talk to your doctor about other medicines to treat your high blood pressure before taking TEKTURNA.

Do not take TEKTURNA if you are allergic to any of its ingredients.

TEKTURNA can cause swelling of the face, lips, tongue, throat, arms and legs, or the whole body. Get medical help right away and tell your doctor if you get any one or more of these symptoms. This reaction, called angioedema, can happen at any time while you are taking TEKTURNA.

Your blood pressure may get too low if you also:

- take water pills (also called "diuretics")
- are on a low-salt diet
- get dialysis treatments
- have heart problems
- get sick with vomiting or diarrhea

Lie down if you feel faint or dizzy. Call your doctor right away.

Tell your doctor about all of your medical conditions, including kidney problems, or whether you have ever had angioedema to an ACE inhibitor medicine.

Also, tell your doctor about all medicines you take, including other medicines for high blood pressure or a heart problem, atorvastatin, water pills, cyclosporine, potassium-containing medicines, potassium supplements, or salt substitutes containing potassium, or medicines to treat fungal infections.

The most common side effects of TEKTURNA include:

- diarrhea

- cough
- dizziness
- headache
- flu-like symptoms
- back pain
- tiredness

Less common side effects include rash.

For full prescribing information, log onto www.pharma.us.novartis.com or contact Christine Cascio at 1-862-778-8026 or christine.cascio@novartis.com.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as "may," "commitment," "dedicated," or similar expressions, or by express or implied discussions regarding potential future revenues from Amturnide. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Amturnide will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Amturnide could be affected by, among other things, competition in general; government, industry and general public pricing pressures; unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; the impact that the foregoing factors could have on the values attributed to the Novartis Group's assets and liabilities as recorded in the Group's consolidated balance sheet, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

Novartis Pharmaceuticals Corporation researches, develops, manufactures and markets innovative prescription drugs used to treat a number of diseases and conditions, including cardiovascular, dermatological, central nervous system, bone disease, cancer, organ transplantation, psychiatry, infectious disease and respiratory. The company's mission is to improve people's lives by pioneering novel healthcare solutions.

Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which provides healthcare solutions that address the evolving needs of patients and societies. Focused solely on healthcare, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic pharmaceuticals, preventive vaccines, diagnostic tools and consumer health products. Novartis is the only company with leading positions in these areas. In 2009, the Group's continuing operations achieved net sales of USD 44.3 billion, while approximately USD 7.5 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 102,000

full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit http://www.novartis.com.

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