Novartis receives FDA approval of Tekamlo™, a single-pill combination of aliskiren and amlodipine to treat high blood pressure

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- -- Tekamlo combines in a single-pill the only approved direct renin inhibitor, Tekturna, with the widely prescribed calcium channel blocker, amlodipine
- -- Data showed Tekamlo significantly reduced blood pressure compared to amlodipine or Tekturna alone
- -- Up to 85 percent of patients may need multiple medications to help control their high blood pressure underscoring the need for effective combination treatments

EAST HANOVER, N.J., Aug. 27 /PRNewswire/ -- The US Food and Drug Administration (FDA) approved Tekamlo™ (aliskiren and amlodipine) tablets, a single-pill for the treatment of high blood pressure combining the only approved direct renin inhibitor, Tekturna® (aliskiren), with the widely used calcium channel blocker amlodipine. Tekamlo is approved as initial therapy for patients who are likely to need multiple drugs to achieve their blood pressure goals, and as replacement therapy for patients whose blood pressure is not adequately controlled with either aliskiren or amlodipine alone.

"We welcome the FDA's decision to approve Tekamlo, as the treatment of high blood pressure remains a challenge for many patients, requiring multiple medications to control their condition," said David Epstein, Division Head of Novartis Pharmaceuticals. "This approval reinforces Novartis' commitment to cardiovascular research and to developing innovative and effective treatments for patients who have not reached their blood pressure goal."

The FDA approval of Tekamlo was based on clinical trial data involving more than 5,000 patients with mild-to-moderate high blood pressure. An eight-week, randomized, double-blind, placebo-controlled, multi-factorial study showed that the combination of Tekturna and amlodipine resulted in decreases in systolic/diastolic blood pressure at trough of 14-17/9-11 mmHg, compared to 4-9/3-4 mmHg for Tekturna alone, and 9-14/6-8 mmHg for amlodipine alone.

In two additional double-blind, active-controlled studies of similar design evaluating patients with moderate-to-severe high blood pressure (SBP 160 - 200 mmHg), Tekamlo demonstrated significantly greater reductions in systolic and diastolic blood pressures when compared to amlodipine alone. In one study of 443 Black patients, the systolic/diastolic treatment difference between Tekamlo and amlodipine was 5.2/3.8 mmHg at the primary endpoint of eight weeks. In the other study of 484 patients, the treatment difference between Tekamlo and amlodipine was 7.1/3.8 mmHg at endpoint.

The single-pill combination Tekamlo works to lower blood pressure in two 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 the blood vessel walls through the inhibition of calcium. Both of these medicines enable blood to flow more easily therefore lowering blood pressure. The blood pressure

lowering effects of Tekamlo are largely attained within one to two weeks.

"Single-pill combination therapies provide a convenient treatment option while supporting physicians in addressing the complex needs of patients," said Alan H. Gradman, M.D., Professor of Medicine at Temple University School of Medicine. "This new single-pill combination demonstrated greater blood pressure reductions than either drug alone in clinical studies and therefore provides a new option to consider when choosing appropriate high blood pressure therapies."

Nearly 75 million -- or one in three -- US adults have hypertension. If left untreated, high blood pressure can lead to stroke, heart attack and heart failure. Tekamlo is not approved to treat or prevent stroke, heart attack and heart failure.

Of US adults being treated with high blood pressure medications, an estimated 31 percent do not have their blood pressure controlled to the recommended target of <140/90 mmHg. Research suggests that up to 85 percent of patients may need multiple medicines to achieve target levels of blood pressure control.

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 effective medicines, programs and an ongoing commitment to research.

Tekamlo is available in four strengths as once-daily tablets containing aliskiren and amlodipine: 150 mg/5 mg tablets, 150 mg/10 mg tablets, 300 mg/5 mg tablets and 300 mg/10 mg tablets.

About Tekamlo

Tekamlo is indicated for the treatment of hypertension, alone or with other antihypertensive agents.

Use Tekamlo as initial therapy in patients who are likely to need multiple drugs to achieve their blood pressure goals. Base the choice of Tekamlo as initial therapy on an assessment of potential benefits and risks. Individualize the decision to use a combination as initial therapy by weighing factors such as baseline blood pressure, the target goal, and the incremental likelihood of achieving goal with a combination compared to monotherapy.

Switch a patient whose blood pressure is not adequately controlled with aliskiren or amlodipine (or another dihydropyridine calcium channel blocker) alone to combination therapy with Tekamlo.

Important Considerations

WARNING: AVOID USE IN PREGNANCY

When pregnancy is detected, discontinue Tekamlo 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) in full Prescribing Information]

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 Tekamlo immediately in patients who develop angioedema and do not readminister.

Excessive hypotension was rarely seen (0.2%) in patients with uncomplicated hypertension treated with Tekamlo in controlled trials. Volume- and/or salt-depletion should be corrected prior to administration of Tekamlo or symptomatic hypotension may occur.

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.

Clinical trials with Tekamlo in hypertension excluded patients with severe renal impairment. Clinical trials of aliskiren in hypertension excluded patients with severe renal dysfunction (GFR <30mL/min). Consider periodic determinations of serum electrolytes to detect possible electrolyte imbalances.

Caution should be exercised when administering Tekamlo to patients with severe renal impairment, as amlodipine is extensively metabolized by the liver and the plasma elimination half-life is 56 hours in patients with impaired hepatic function.

Titrate Tekamlo slowly in patients with heart failure.

No data are available on the use of Tekamlo or aliskiren in patients with unilateral or bilateral renal artery stenosis. However, 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.

Exercise caution when co-administering Tekamlo with ACEIs, potassium-sparing diuretics, potassium supplements, or other potassium containing salt substitutes.

Concomitant use of Tekamlo with cyclosporine is not recommended.

The most common adverse event in a placebo-controlled trial that occurred in at least 2% of patients treated with Tekamlo and at a higher incidence than placebo was peripheral edema (6.2% vs 1.0%). The incidence rate of peripheral edema at high dose was 8.9%.

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 "commitment," "in development," "dedicated," or similar expressions, or by express or implied discussions regarding potential future approvals of Tekamlo in additional markets, regarding the potential development of other single-pill combinations with aliskiren, or regarding potential future revenues from Tekamlo, Tekturna or other combination products containing aliskiren. 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 Tekamlo will be approved for sale in any additional markets. Nor can there be any guarantee that Novartis will successfully develop any additional single-pill combination products containing aliskiren. Neither can there be any guarantees that Tekamlo, Tekturna or other combination products containing aliskiren will achieve any particular levels of revenue in the future. In particular, management's expectations regarding such products could be affected by, among other things, 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; competition in general; government, industry and general public pricing pressures; 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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