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FDA Approves Tekturna HCT® as Initial Treatment in Patients Unlikely to Achieve Their Blood Pressure Goals With a Single Agent

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- - Tekturna HCT combines the only approved direct renin inhibitor, Tekturna®, with widely used diuretic, hydrochlorothiazide, in a single pill
- - Data show combination of Tekturna and hydrochlorothiazide resulted in significant additional blood pressure reductions compared to either drug alone
- - Research suggests up to 85% of patients need multiple medications to help reach blood pressure goals, underscoring the need for effective combination treatments
- - Medical guidelines recommend consideration for combination therapy first in patients unlikely to get to goal with a single agent

EAST HANOVER, N.J., July 21 /PRNewswire/ -- The US Food and Drug Administration (FDA) has approved Tekturna HCT(®) (aliskiren and hydrochlorothiazide) tablets as initial therapy for patients who are likely to need multiple drugs to achieve their blood pressure goals. Tekturna HCT is a single-pill combination of Tekturna(®) (aliskiren), the first and only approved direct renin inhibitor, and the diuretic hydrochlorothiazide (HCTZ), one of the most commonly-used high blood pressure medications.

The FDA approval of Tekturna HCT as initial therapy was based on clinical trial data involving more than 2,700 patients, which showed that treatment with the combination of Tekturna and HCTZ offered greater blood pressure reductions than either drug alone.

"Up to 85% of patients will need more than one medication to reach their blood pressure goals," said Alan Gradman, MD, Cardiologist at The Western Pennsylvania Hospital and Professor of Medicine at Temple University. "This approval gives doctors the opportunity to aggressively treat their patients with a single-pill combination of the only approved drug, Tekturna, that works by directly targeting renin and decreasing the activity of the renin angiotensin aldosterone system (RAAS) and, HCTZ, a diuretic. This results in more significant blood pressure reductions, compared to taking either drug alone."

Hypertension affects nearly 74 million US adults and is a major risk factor for cardiovascular disease, the number one leading cause of death in the US. If left untreated, patients with high blood pressure are at risk for cardiovascular events such as stroke, heart attack and heart failure. Of US adults being treated, an estimated 36% are not at their blood pressure goals.

Current US treatment guidelines support the first-line use of combination therapy in appropriate high blood pressure patients. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) recommends that physicians consider starting their high blood pressure patients with two treatment agents, one of which should be a diuretic, if blood pressure is >20/10 mmHg above goal. The use of multiple medications may help patients achieve blood pressure goals in a more timely fashion.

"We are very pleased the FDA recognizes the benefit of Tekturna HCT for the first-line treatment of patients

with moderately high blood pressure," said Trevor Mundel, MD, Global Head of Development at Novartis Pharma AG. "Novartis is committed to supporting the research and development of effective treatments for high blood pressure that will help patients reach their blood pressure treatment goals."

Tekturna, a direct renin inhibitor, is the only drug that works by directly targeting renin and decreasing the activity of the RAAS. Renin is an enzyme produced by the kidneys that starts a process that makes blood vessels narrow and, when inappropriately activated, may lead to high blood pressure. Tekturna reduces renin activity and helps blood vessels relax and widen so blood pressure is lowered. Diuretics work to lower blood pressure by removing excess water and salt from the body.

Tekturna was approved in the US in 2007 as the first direct renin inhibitor. In 2008, Tekturna HCT was approved in the US for second-line treatment of high blood pressure. The long-term potential of Tekturna is being studied in an extensive clinical program, including outcomes trials, known as ASPIRE HIGHER.

Tekturna HCT is available in four strengths as tablets containing aliskiren and hydrochlorothiazide: 150 mg/12.5 mg tablets, 150 mg/25 mg tablets, 300 mg/12.5 mg tablets and 300 mg/25 mg tablets.

Study details

The FDA approvals of Tekturna HCT were based on a clinical trial program involving over 6,200 patients and evaluated more than 2,700 patients exposed to combinations of Tekturna and hydrochlorothiazide. The safety and efficacy of Tekturna HCT were evaluated in patients with mild-to-moderate hypertension in an 8-week, randomized, double-blind, placebo-controlled, parallel-group, 15-arm factorial trial (n=2762). Patients were randomized to receive various combinations of Tekturna (75 mg to 300 mg) plus hydrochlorothiazide (6.25 mg to 25 mg) once daily (without titrating up from monotherapy) and followed for blood pressure response. The combination of Tekturna and hydrochlorothiazide resulted in additive placebo-adjusted decreases in systolic and diastolic blood pressure at trough of 10-14/5-7 mmHg at doses of 150-300 mg/12.5-25 mg, compared to 5-8/2-3 mmHg for Tekturna 150 mg to 300 mg and 6-7/2-3 mmHg for hydrochlorothiazide 12.5 mg to 25 mg alone. Blood pressure reductions with the combinations were greater than the reductions with the monotherapies. The safety and efficacy of Tekturna HCT as initial therapy was evaluated in this trial. All patients randomized to the combination groups received the combination treatment of Tekturna HCT at assigned doses as initial therapy without titration from monotherapy. The antihypertensive effect of Tekturna HCT were largely manifested within 1 week. The maximum antihypertensive effect was generally attained after about 4 weeks of therapy.

About Tekturna and Tekturna HCT

TEKTURNA and TEKTURNA HCT are prescription medications for adults used to treat high blood pressure. TEKTURNA and TEKTURNA HCT may be used alone or in combination with other high blood pressure medications. It is not known whether additive effects are present when TEKTURNA or TEKTURNA HCT are used in combination with types of medications called ACE inhibitors or beta-blockers. TEKTURNA HCT can be used first if your doctor thinks you are unlikely to achieve your goal blood pressure with a single medicine.

Important considerations

IMPORTANT WARNING:

TEKTURNA or TEKTURNA HCT may harm an unborn baby, causing injury and even death. If you get pregnant, stop taking TEKTURNA or TEKTURNA HCT 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 or TEKTURNA HCT.

Do not take TEKTURNA or TEKTURNA HCT if you are allergic to any of its ingredients. Do not take TEKTURNA HCT if you have a history of reduced urine output, or if you have allergic reactions to certain drugs known as sulfonamides. If you are taking TEKTURNA or TEKTURNA HCT, tell your doctor about all of your medical conditions, including kidney problems. Also, tell your doctor about all medicines you take, including those to treat fungal infections, cyclosporine, potassium-containing medicines, potassium supplements, or salt substitutes containing potassium. Additionally, if you take TEKTURNA HCT, tell your doctor if you have liver problems, lupus, or if you take lithium.

Two of the most serious side effects of TEKTURNA and TEKTURNA HCT include an allergic reaction involving swelling of the face, lips, throat and/or tongue that may cause difficulty in breathing and swallowing (stop taking TEKTURNA or TEKTURNA HCT and contact your doctor immediately), and low blood pressure, especially if you take water pills, are on a low-salt diet, get dialysis treatments, have heart problems, or get sick with vomiting or diarrhea. Lie down if you feel faint or dizzy. Call your doctor right away.

In clinical studies, the most common side effect experienced by more patients taking TEKTURNA than patients taking a sugar pill was diarrhea. The most common side effects experienced by more patients taking TEKTURNA HCT than a sugar pill included dizziness, flu-like symptoms, diarrhea, cough, and tiredness. Other less common reactions to TEKTURNA and TEKTURNA HCT include skin rash and, additionally with TEKTURNA, cough.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as "may," "will," "risk," "estimated," "committed," "potential," or similar expressions, or by express or implied discussions regarding potential future indications or labeling for Tekturna or Tekturna HCT, or regarding potential future revenues from Tekturna or Tekturna HCT. 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 Tekturna or Tekturna HCT will be approved for any additional indications or labeling. Nor can there be any guarantee that Tekturna or Tekturna HCT will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Tekturna and Tekturna HCT could be affected by, among other things, unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; competition in general; unexpected regulatory actions or delays or government regulation generally; 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 Pharmaceuticals Corporation

Novartis Pharmaceuticals Corporation researches, develops, manufactures and markets leading innovative prescription drugs used to treat a number of diseases and conditions, including those in the cardiovascular, metabolic, cancer, organ transplantation, central nervous system, dermatological, GI and respiratory areas.

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, preventive vaccines, diagnostic tools, cost-saving generic pharmaceuticals, and consumer health products. Novartis is the only company with leading positions in these areas. In 2008, the Group's continuing operations achieved net sales of USD 41.5 billion and net income of USD 8.2 billion. Approximately USD 7.2 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 98,000 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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* Tekturna® is the US trade name for aliskiren. Aliskiren is known as Rasilez® outside the US.

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