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Video: FDA approves Exforge HCT® - the Only High Blood Pressure Treatment to Combine Three Medications in a Single Pill

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- Exforge HCT combines a proven calcium channel blocker, angiotensin receptor blocker and diuretic (amlodipine, valsartan, hydrochlorothiazide) in one pill

- In a clinical trial, Exforge HCT demonstrated significantly greater reductions in systolic and diastolic BP, compared to all dual combinations of its components

- Up to 85% of patients may need multiple medications to help control their blood pressure and many need three or more

- Exforge HCT can help appropriate patients reach BP goals; offers convenience and potential cost savings by reducing up to three co-payments to one

EAST HANOVER, N.J., April 30 /PRNewswire/ -- The US Food and Drug Administration (FDA) has approved Exforge HCT (amlodipine, valsartan, hydrochlorothiazide), the only blood pressure (BP) treatment to combine three medications in a single pill. Exforge HCT combines the number one prescribed calcium channel blocker, angiotensin receptor blocker, and diuretic in one pill, and is an important new option for patients who have tried taking dual combinations of these classes of blood pressure medications without success.

To view the Multimedia News Release, go to: http://www.prnewswire.com/mnr/exforge/38191/

"The majority of people with hypertension will require more than one medication to control their blood pressure and it's not uncommon for patients with severe hypertension and/or patients requiring stricter blood pressure control to need three or more medications," said David A. Calhoun, MD, Professor of Medicine, Vascular Biology and Hypertension Program, University of Alabama at Birmingham. "With a triple combination option, appropriate patients may experience a simpler routine of a convenient, once-daily pill to help them control their high blood pressure."

Exforge HCT provides proven efficacy in patients with moderate to severe hypertension (MSDBP greater than

or equal to 100 mmHg and <120 mmHg, MSSBP greater than or equal to 145 mmHg and <200 mmHg). In a clinical trial, the maximum dose of Exforge HCT (amlodipine/valsartan/ hydrochlorothiazide 10 mg/320 mg/25 mg) demonstrated significantly greater reductions in systolic and diastolic blood pressures when compared to all dual combinations of its components at the same doses (valsartan/hydrochlorothiazide 320 mg/25 mg, amlodipine/valsartan 10 mg/320 mg, and amlodipine/hydrochlorothiazide 10 mg/25 mg), providing additional reductions of 18-29% in systolic blood pressure and 19-32% in diastolic blood pressure. The reductions in systolic/diastolic blood pressure with Exforge HCT were 7.6/5.0 mmHg greater than with valsartan/hydrochlorothiazide, 6.2/3.3 mmHg greater than with amlodipine/valsartan, and 8.2/5.3 mmHg greater than with amlodipine/hydrochlorothiazide. These results also include a placebo effect of unknown size. Ambulatory blood pressure monitoring showed that the blood pressure lowering effect of Exforge HCT was maintained throughout the 24-hour period.

High blood pressure affects approximately 74 million adults in the US and one in four adults worldwide. If high blood pressure is not treated, it can lead to heart attack and stroke. Exforge HCT is not indicated for the treatment or prevention of heart attack or stroke.

Research suggests that up to 85% of patients may need multiple medications and many need three or more to help control their blood pressure. Patients may find treatment more convenient with one single pill rather than separate pills.

Exforge HCT contains three effective medicines that work in three different ways. A patient may be switched to the single pill combination Exforge HCT if blood pressure is not adequately controlled on any two of the following anti-hypertensive classes: calcium channel blockers, angiotensin receptor blockers, and diuretics. The full blood pressure lowering effect was achieved two weeks after being on the maximal dose of Exforge HCT.

Exforge and Exforge HCT will be offered at the same price in the US on a dose-equivalent basis, essentially providing the added diuretic in Exforge HCT at no additional cost. Since Exforge HCT combines three medications in a single pill, patients may benefit from reduced insurance co-payments.

"This approval of Exforge HCT as the only single blood pressure pill combining the efficacy of three of the most-prescribed treatments in their classes represents a significant milestone toward reducing the burden of unmet need in hypertension," said Trevor Mundel, MD, Global Head of Development at Novartis Pharma AG. "Novartis remains confident in the important role of single pill combination medications to help appropriate patients achieve their blood pressure targets, while providing physicians with a range of powerful yet flexible combinations of doses to effectively manage high blood pressure in different patients."

This FDA approval was based on a clinical trial of Exforge HCT of over 2,000 patients.

Indications and Important Safety Information

EXFORGE® is indicated for the treatment of hypertension in patients not adequately controlled on monotherapy and as initial therapy in patients likely to need multiple drugs to reach their blood pressure goals.

The decision to use a combination as initial therapy should be individualized and should be shaped by considerations such as baseline blood pressure, the target goal, and the incremental likelihood of achieving goal with a combination product compared to monotherapy.

EXFORGE HCT® is indicated for the treatment of hypertension. This fixed combination drug is not indicated for the initial therapy of hypertension.

IMPORTANT CONSIDERATIONS

WARNING: AVOID USE IN PREGNANCY: When pregnancy is detected, discontinue EXFORGE or EXFORGE HCT as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury or death to the developing fetus. [See Warnings and Precautions (5.1)]

Because of the hydrochlorothiazide component, EXFORGE HCT is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

Excessive hypotension was seen in 0.4% of patients treated with EXFORGE and in 1.7% of patients treated with EXFORGE HCT 10/320/25 mg. Correct volume- or salt-depletion before administering EXFORGE or EXFORGE HCT or symptomatic hypotension may occur. Caution should be observed when initiating therapy with EXFORGE in patients with heart failure or recent myocardial infarction and in patients undergoing surgery or dialysis. Do not initiate treatment with EXFORGE HCT in patients with aortic or mitral stenosis or obstructive hypertrophic cardiomyopathy.

Rarely, increased frequency, duration, or severity of angina or acute myocardial infarction have developed in patients treated with calcium channel blockers; particularly patients with severe obstructive coronary artery disease.

EXFORGE should be used with caution in patients with severe hepatic impairment and should be used with care in patients with mild-to-moderate hepatic impairment, including patients with biliary obstructive disorders, because of lower valsartan clearance.

Avoid use of EXFORGE HCT in patients with severe hepatic impairment. In patients with mild-to-moderate hepatic impairment, including patients with biliary obstructive disorders, monitor for worsening of hepatic or renal function, including fluid status and electrolytes, and adverse reactions.

In patients with renal artery stenosis or severe renal impairment, care should be exercised with dosing of EXFORGE. Avoid use of EXFORGE HCT in severe renal disease (creatinine clearance less than or equal to 30 mL/min). The usual regimens of therapy with EXFORGE HCT may be followed if the patient's creatinine clearance is >30 mL/min.

In patients with severe heart failure, decline in renal function and rarely, acute renal failure and/or death has been associated with inhibiting the renin-angiotensin system. Evaluation of patients with heart failure or post-myocardial infarction should always include assessment of renal function. Dosage reduction and/or discontinuation of the diuretic and/or valsartan may be required.

Important considerations due to the hydrochlorothiazide component of EXFORGE HCT: Thiazides have been reported to cause exacerbation or activation of systemic lupus erythematosus. Lithium generally should not be given with thiazides.

Monitor serum electrolytes periodically based on EXFORGE HCT use and other factors such as renal function, other medications, or history of prior electrolyte imbalances.

The most common adverse reactions that occurred more frequently with EXFORGE than placebo were peripheral edema (5% vs 3%), nasopharyngitis (4% vs 2%), upper respiratory tract infection (3% vs 2%), and dizziness (2% vs 1%).

The most frequent adverse events that occurred in greater than or equal to 2% of patients treated with EXFORGE HCT were dizziness (8.2%), edema (6.5%), headache (5.2%), dyspepsia (2.2%), fatigue (2.2%), muscle spasms (2.2%), back pain (2.1%), nausea (2.1%) and nasopharyngitis (2.1%).

Please see accompanying full Prescribing Information.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as "may," "can," "potential," "will," "confident," "likely," "likelihood," or similar expressions, or by express or implied discussions regarding potential future revenues from Exforge 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

with Exforge HCT to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Exforge HCT will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Exforge HCT 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 Pharmaceuticals Corporation

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 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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