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Novartis' new heart failure medicine LCZ696 approved by FDA to reduce risk of cardiovascular death and heart failure hospitalization; now called Entresto™ (sacubitril/valsartan)

Jul 07, 2015

- - First in the world approval brings hope of longer life and fewer HF hospitalizations by reducing the devastating impact of heart failure with reduced ejection fraction for millions of patients in the US1-3
- - Entresto is the first and only treatment to show a significant mortality benefit in a head-to-head trial against ACE-inhibitor enalapril4
- - Heart failure is a life-threatening condition affecting nearly 6 million Americans; about half have the reduced ejection fraction form2,3,5
- - Approval comes six weeks ahead of FDA's priority review action date; Novartis is working to make Entresto available to patients as quickly as possible

EAST HANOVER, N.J., July 7, 2015 /PRNewswire/ -- Novartis announced today that the US Food and Drug Administration (FDA) has approved Entresto™ (sacubitril/valsartan) tablets, previously known as LCZ696, to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction (HFrEF). It is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other angiotensin receptor blocker (ARB).[1] Reduced ejection fraction means the heart doesn't contract with enough force, so less blood is pumped out.[6]

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"The approval of Entresto marks a new era in the treatment of heart failure made possible by the collective efforts of our Novartis associates, the hundreds of cardiologists and nurses, and thousands of patients who participated in the research," said Christi Shaw, US Country Head, President of Novartis Corporation and Novartis Pharmaceuticals Corporation. "We have so many people in the heart failure community to thank for helping bring this exciting new treatment to patients and are working hard to make it available at pharmacies as quickly as possible."

The FDA's decision is based on results from the 8,442-patient PARADIGM-HF study, the largest clinical trial ever conducted in heart failure.[1,7] In the study, Entresto demonstrated clinically relevant and statistically significant superiority to ACE-inhibitor enalapril, reducing the risk of cardiovascular death or heart failure hospitalization by 20% (the primary endpoint) at a median follow-up of 27 months. Entresto also improved overall survival by 16% versus enalapril, driven by the lower incidence of cardiovascular death.[1,4] The study was stopped early after the Data Monitoring Committee overseeing the study found that Entresto significantly reduced the risk of cardiovascular death and that the primary endpoint had been met.[8]

"The very meaningful survival advantage of Entresto seen in the PARADIGM-HF trial should persuade physicians to consider Entresto for all appropriate patients, in place of traditional ACE inhibitors or angiotensin receptor blockers," said Dr. Milton Packer, Professor and Chair for the Department of Clinical Sciences at University of Texas Southwestern Medical Center, Texas, USA. "Entresto is expected to change the management of patients with

HFrEF for years to come."

Nearly 6 million people in the United States suffer from heart failure and about half have the reduced ejection fraction form.[2,3] Up to 2.2 million of these patients have heart failure classified as NYHA II-IV, based on how much their symptoms limit physical activity.[9,10] Heart failure is a debilitating and life-threatening condition in which the heart cannot pump enough blood around the body.[5] Patients face a high risk of death, repeated hospitalizations and symptoms such as breathlessness, fatigue and fluid retention that significantly impact quality of life.[5,11-14]

"Heart failure places a tremendous physical, emotional and financial burden on patients, their caregivers and society," said Michele Blair, Chief Executive Officer at the Heart Failure Society of America. "There is a great need in the heart failure community for therapies that improve patient outcomes. Today's approval is a victory for patients, and we welcome the addition of a new treatment option to help manage this very serious condition."

About Heart Failure
Heart failure represents a major and growing health-economic toll that currently exceeds $30 billion in the United States, accounting for both direct and indirect costs. Hospitalizations account for 80% of the $21 billion spent on the direct costs of heart failure.[15] Some 870,000 new heart failure patients are diagnosed annually.[2] With the aging population, it is estimated over 8 million Americans will have heart failure by 2030.[15] It is the most common reason people over 65 go into the hospital, and overall it accounts for more than 1 million hospitalizations each year.[2,16] Despite available therapies, nearly half of heart failure patients die within 5 years of diagnosis.[13,14]

About Entresto
Entresto is a twice-a-day medicine that reduces the strain on the failing heart. It does this by enhancing the protective neurohormonal systems of the heart (NP system) while simultaneously suppressing the harmful effects of the overactive renin-angiotensin-aldosterone system (RAAS).[1] Other heart failure medicines only block the harmful effects of the overactive RAAS.[10] Entresto contains the neprilysin inhibitor sacubitril, which is a new molecular entity, and the angiotensin receptor blocker (ARB) valsartan.[1]

Entresto film-coated tablets are available in three dosage strengths: 24/26 mg, 49/51 mg, and 97/103 mg (sacubitril/valsartan).[1] These doses are referred to as 50 mg, 100 mg, and 200 mg in the clinical trial literature including the New England Journal of Medicine publication of the results of PARADIGM-HF. The target dose of Entresto is 97/103 mg twice daily.[1]

Patient Access and Support
Novartis is committed to providing patients with affordable access and resources through Entresto Central, a program offering personalized reimbursement services such as assistance with health insurance questions, the Entresto prescription co-pay programs for eligible patients including a one-time free trial offer, and the Novartis US Patient Assistance Foundation, Inc. Novartis also supports independent charitable foundations that provide financial assistance for eligible, insured patients who need help paying their out-of-pocket medication costs. For more information, please call 1-888-ENTRESTO or visit www.entresto.com.

Please visit http://www.pharma.us.novartis.com/product/pi/pdf/entresto.pdf for Entresto full Prescribing Information.

IMPORTANT SAFETY INFORMATION
Entresto can harm or cause death to an unborn baby. Patients should talk to their doctor about other ways to treat heart failure if they plan to become pregnant. If a patient gets pregnant while taking Entresto, she should tell her doctor right away.

Patients are not to take Entresto if they are allergic to sacubitril or valsartan or any of the ingredients in Entresto; have had an allergic reaction including swelling of the face, lips, tongue, throat or trouble breathing while taking a type of medicine called angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB); or

take an ACE inhibitor medicine. Patients are not to take Entresto for at least 36 hours before or after they take an ACE inhibitor medicine. Patients should talk with their doctor or pharmacist before taking Entresto if they are not sure if they take an ACE inhibitor medicine. Patients are not to take Entresto if they have diabetes and take a medicine that contains aliskiren.

Before they take Entresto, patients should tell their doctor about all of their medical conditions, including if they have kidney or liver problems; are pregnant or plan to become pregnant; are breastfeeding or plan to breastfeed. Patients should either take Entresto or breastfeed. They should not do both.

Patients should tell their doctor about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. They should especially tell their doctor if they take potassium supplements or a salt substitute; nonsteroidal anti-inflammatory drugs (NSAIDs); lithium; or other medicines for high blood pressure or heart problems such as an ACE inhibitor, ARB, or aliskiren.

Entresto may cause serious side effects including serious allergic reactions causing swelling of the face, lips, tongue, and throat (angioedema) that may cause trouble breathing and death. Patients are to get emergency medical help right away if they have symptoms of angioedema or trouble breathing. Patients are not to take Entresto again if they have had angioedema while taking Entresto. People who are black or who have had angioedema may have a higher risk of having angioedema if they take Entresto. Entresto may cause low blood pressure (hypotension). Patients are to call their doctor if they become dizzy or lightheaded, or they develop extreme fatigue. Entresto may cause kidney problems or an increased amount of potassium in the blood.

The most common side effects were low blood pressure, high potassium, cough, dizziness, and kidney problems.

Please see full Prescribing Information, including Boxed WARNING available at http://www.pharma.us.novartis.com/product/pi/pdf/entresto.pdf.

Patients are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as "hope," "working," "as quickly as possible," "exciting," "should," "expected," "for years to come," "growing," "will," "committed," or similar terms, or by express or implied discussions regarding potential additional marketing approvals or new indications or labeling for Entresto, or regarding potential future revenues from Entresto. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that Entresto will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Neither can there be any guarantee that Entresto will be submitted or approved for sale in any additional markets or at any particular time. Nor can there be any guarantee that Entresto will be commercially successful in the future. In particular, management's expectations regarding Entresto could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected manufacturing issues, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. 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 medicines aimed at improving patients' lives. We offer a broad range of medicines for cancer, cardiovascular disease, endocrine disease, inflammatory disease, infectious disease, neurological disease, organ transplantation, psychiatric disease, respiratory disease and skin conditions. 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 innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2014, the Group achieved net sales of USD 58.0 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 120,000 full-time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit http://www.novartis.com.

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