Novartis Entresto® granted expanded indication in chronic heart failure by FDA

Feb 16, 2021

- Entresto is the first and only therapy approved in the US to treat patients diagnosed with guideline-defined heart failure to include both those with heart failure with reduced ejection fraction (HFrEF) and many with heart failure with preserved ejection fraction (HFpEF)(1-3)
- Expanded indication enables potential treatment of more adults with left ventricular ejection fraction (LVEF) below normal, the group where benefits are most clearly evident(1)
- Of the more than 6 million Americans suffering from chronic heart failure (CHF), approximately 5 million may be appropriate for treatment with Entresto(3,4)

EAST HANOVER, N.J., Feb. 16, 2021 -- Novartis today announced that the US Food and Drug Administration (FDA) has approved the following expanded indication for Entresto® (sacubitril/valsartan): to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure.[1] Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal.[1] The label also states LVEF is a variable measure and clinical judgment should be used in deciding whom to treat.[1]

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For the first time, there is a treatment with benefit for patients diagnosed with guideline-defined heart failure that includes both those with heart failure with reduced ejection fraction (HFrEF) and many with heart failure with preserved ejection fraction (HFpEF).[1-3]

"This approval is a significant advancement, providing a treatment to many patients who were not eligible for treatment before because their ejection fraction was above the region we normally considered reduced. Until now, treatment for these patients was largely empiric," said Scott Solomon, MD, Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital, and PARAGON-HF Executive Committee Co-Chair. "We can now offer a treatment to a wider range of patients who have an LVEF below normal."

This label expansion is based on efficacy and safety evidence observed in PARAGON-HF, the largest and only Phase III active-controlled study to date in patients with guideline-defined HFpEF.[2,5,6] The greatest benefit was shown in patients with LVEF below normal.[6]

Approximately 6 million Americans are living with chronic heart failure (CHF).[4] Approximately 3 million have HFrEF, and of the remaining 3 million, about 2 million have HFpEF with LVEF below normal.[2-4] The prevalence of heart failure (HF) is increasing as the population ages.[4] Patients often face worsening symptoms that result in frequent HF hospitalizations.[7] Each hospitalization event is associated with worsening long-term prognosis.[7] Approximately one in four patients are re-admitted for HF and 10 percent may die within 30 days of discharge.[8,9] Overall CHF death rates remain significantly high, with up to half of patients dying within five years of a HF diagnosis.[4]

"We are proud of our goal to reimagine medicine. This commitment has enabled us to bring Entresto to

millions more heart failure patients in the US, many of whom did not have an approved treatment option until now," said Marie-France Tschudin, President, Novartis Pharmaceuticals. "This achievement would not have been possible without tremendous dedication from investigators, patients in our clinical trials and the advocacy community, to whom we are extremely grateful."

About our longstanding commitment to heart failure

Our goal is to reimagine medicine for heart failure patients. Novartis established the largest global clinical program in the HF disease area across the pharma industry to date. Known as FortiHFy, it is comprised of more than 40 clinical studies designed to generate an array of additional data on efficacy, quality of life, patient-reported outcomes and real-world evidence with Entresto, as well as to extend understanding of heart failure. FortiHFy includes trials across the spectrum of heart failure, such as PARADIGM-HF, PIONEER-HF, TRANSITION, PROVE-HF, PARAGON-HF and PARAMOUNT. Worldwide, it is estimated that more than 30,000 patients have participated in the Entresto clinical trials program, and it is estimated that more than 2.8 million patients are on treatment with Entresto today.

About Entresto

Entresto (sacubitril/valsartan) is a prescription medicine to treat adults with long-lasting (chronic) heart failure to help reduce the risk of death and hospitalization. Entresto works better when the heart cannot pump a normal amount of blood to the body.[1] Entresto is a twice-a-day prescription medicine that works by enhancing the beneficial neurohormonal systems (natriuretic peptide system) while simultaneously inhibiting the harmful effects of the overactive renin-angiotensin-aldosterone system (RAAS).[1,10] Some other heart failure medicines only block the harmful effects of the overactive RAAS. Entresto contains the neprilysin inhibitor sacubitril and the 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.[1] In adult patients, the target maintenance dose of Entresto is 97/103 mg twice daily as tolerated by the patient.[1]

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 during treatment with Entresto, she should tell her doctor right away.

Patients should not take Entresto if they are allergic to 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 an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB); or take an ACE inhibitor medicine. Patients should not 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 should not 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 a history of hereditary angioedema; 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 should 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), which may be more common if you take water pills. 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 (hyperkalemia).

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

Please see full Prescribing Information, including Boxed WARNING available at https://www.novartis.us/sites/www.novartis.us/files/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.

Novartis is committed to providing patients with affordable access and resources through Entresto Central. For more information, please call 1-888-ENTRESTO or visit www.entresto.com.

About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of Novartis – is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs nearly 16,000 people in the United States. For more information, please visit https://www.novartis.us.

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