



NEWS RELEASE

Merck Announces U.S. FDA Approval of VERQUVO® (vericiguat)

1/20/2021

VERQUVO Approved for Reduction of Risk of Cardiovascular Death and Heart Failure (HF) Hospitalization Following a Hospitalization for HF or Need for Outpatient Intravenous (IV) Diuretics in Adults with Symptomatic Chronic Heart Failure and Ejection Fraction Less than 45%

VERQUVO is the First Soluble Guanylate Cyclase Stimulator, Approved to Treat Heart Failure

KENILWORTH, N.J.--(BUSINESS WIRE)-- Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has approved VERQUVO, a soluble guanylate cyclase (sGC) stimulator, to reduce the risk of cardiovascular death and heart failure hospitalization following a hospitalization for heart failure or need for outpatient intravenous (IV) diuretics in adults with symptomatic chronic heart failure and ejection fraction less than 45%. The approval of VERQUVO by the FDA, which is the first treatment for chronic heart failure approved specifically for patients following a hospitalization for heart failure or need for outpatient IV diuretics, is based on the results of the pivotal Phase 3 VICTORIA trial and follows a priority regulatory review. VERQUVO (vericiguat) 2.5 mg, 5 mg, and 10 mg tablets is being jointly developed with Bayer AG.

The VERQUVO label contains a boxed warning that indicates that VERQUVO should not be administered to pregnant females because it may cause fetal harm. For more information, see "Selected Safety Information" below.

"Patients with symptomatic chronic heart failure and reduced ejection fraction have a high risk for hospitalization after experiencing symptoms of heart failure requiring outpatient IV diuretic treatment or hospitalization. By some



estimates, more than half of these patients are rehospitalized within a month of discharge due to a worsening event and approximately one in five die within two years,” said Dr. Paul W. Armstrong, cardiologist and Distinguished University Professor of Medicine at the Canadian VIGOUR Centre, University of Alberta, and study chair of the VICTORIA trial. “The approval of VERQUVO provides doctors, health care professionals, and patients with a welcome new option to current available therapies.”

In VICTORIA, the primary efficacy objective was to determine whether VERQUVO is superior to placebo, both in combination with other heart failure therapies, in reducing the risk of cardiovascular death or heart failure hospitalization in adults with symptomatic chronic heart failure and ejection fraction less than 45% following a worsening heart failure event. VERQUVO met the primary efficacy objective based on a time-to-event analysis (hazard ratio [HR]: 0.90, 95% confidence interval [CI], 0.82-0.98; $p=0.019$). Over the course of the study, there was a 4.2% reduction in annualized absolute risk with VERQUVO compared with placebo. Therefore, 24 patients would need to be treated over an average of one year to prevent one primary endpoint event.

“VERQUVO has been shown to reduce the risk of cardiovascular death and heart failure hospitalization following a hospitalization for heart failure or need for outpatient IV diuretics. We are pleased to offer a meaningful new treatment option for appropriate patients with symptomatic chronic heart failure,” said Dr. Roy Baynes, senior vice president and head of global clinical development, chief medical officer, Merck Research Laboratories. “This approval builds upon Merck’s proud history of developing therapies for the treatment of patients with cardiovascular disease.”

Data Supporting the Approval

The approval of VERQUVO was based on data from VICTORIA (NCT02861534), a randomized, parallel-group, placebo-controlled, double-blind, event-driven, multi-center clinical trial comparing VERQUVO to placebo in 5,050 adult patients with symptomatic chronic heart failure (New York Heart Association [NYHA] class II-IV) and left ventricular ejection fraction (LVEF) less than 45%, following a worsening heart failure event. A worsening heart failure event was defined as heart failure hospitalization within six months or less prior to randomization or use of outpatient IV diuretics for heart failure within three months or less prior to randomization. In VICTORIA, the primary endpoint was a composite of time to first event of cardiovascular death or hospitalization for heart failure. The median follow-up for the primary endpoint was 11 months. VERQUVO was superior to placebo in reducing the risk of cardiovascular death or heart failure hospitalization based on a time-to-event analysis.

Patients received up to the target maintenance dose of VERQUVO 10 mg once daily or matching placebo. Therapy was initiated at VERQUVO 2.5 mg once daily and increased in approximately two-week intervals to 5 mg once daily and then 10 mg once daily, as tolerated. Placebo doses were similarly adjusted. After approximately one year, 90% of patients in both the VERQUVO and placebo arms were treated with the 10 mg target maintenance dose.

Study participants were: 76% male, 64% Caucasian, 22% Asian, and 5% Black. The mean age was 67 years. At randomization, 59% of patients were NYHA Class II, 40% were NYHA Class III and 1% were NYHA Class IV. The mean LVEF was 29%. Approximately half of all patients had an EF less than 30%, and 14% of patients had an EF between 40% and 45%. Sixty-seven percent of the patients in VICTORIA were enrolled within three months of a heart failure hospitalization index event; 17% were enrolled within three to six months of heart failure hospitalization, and 16% were enrolled within three months of outpatient treatment with IV diuretics for worsening heart failure. The median NT-pro B-type natriuretic peptide (NT-proBNP) level was 2800 pg/mL at randomization.

Study participants were on standard of care. At baseline, 93% of patients were receiving a beta-blocker, 73% were receiving an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB), 70% were receiving a mineralocorticoid receptor antagonist (MRA), 15% were receiving a combination of an angiotensin receptor and neprilysin inhibitor (ARNI), 28% had an implantable cardiac defibrillator and 15% had a biventricular pacemaker. Ninety-one percent of patients were treated with two or more heart failure medications (beta blocker, any renin-angiotensin system [RAS] inhibitor or MRA) and 60% of patients were treated with all three. At baseline, 6% of patients were receiving ivabradine and 3% a sodium glucose co-transporter 2 (SGLT2) inhibitor.

In the VICTORIA trial, VERQUVO demonstrated an adverse event profile similar to placebo. The adverse drug reactions occurring more commonly with VERQUVO than placebo and in greater than or equal to 5% of patients treated with VERQUVO in VICTORIA were hypotension (16% vs 15%) and anemia (10% vs 7%). The VICTORIA trial included a total of 2,519 patients treated with VERQUVO (up to 10 mg once daily). The mean duration of VERQUVO exposure was one year, and the maximum duration was 2.6 years.

About VERQUVO® (vericiguat) tablets for once daily oral use (2.5 mg, 5 mg and 10 mg)

Vericiguat is a stimulator of soluble guanylate cyclase (sGC), an important enzyme in the nitric oxide (NO) signaling pathway. When NO binds to sGC, the enzyme catalyzes the synthesis of intracellular cyclic guanosine monophosphate (cGMP), a second messenger that plays a role in the regulation of vascular tone, cardiac contractility, and cardiac remodeling. Heart failure is associated with impaired synthesis of NO and decreased activity of sGC, which may contribute to myocardial and vascular dysfunction. By directly stimulating sGC, independently of and synergistically with NO, vericiguat augments levels of intracellular cGMP, leading to smooth muscle relaxation and vasodilation.

Selected Safety Information for VERQUVO

WARNING: EMBRYO-FETAL TOXICITY

Females of reproductive potential: Exclude pregnancy before the start of treatment. To prevent pregnancy, females of reproductive potential must use effective forms of contraception during treatment and for one month after stopping treatment. Do not administer VERQUVO to a pregnant female because it may cause fetal harm.

VERQUVO is contraindicated in patients with concomitant use of other soluble guanylate cyclase (sGC) stimulators. VERQUVO is contraindicated in pregnancy. Based on data from animal reproduction studies, VERQUVO may cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential of the potential risk to a fetus. Obtain a pregnancy test before the start of treatment. Advise females of reproductive potential to use effective contraception during treatment with VERQUVO and for at least one month after the final dose.

In a clinical trial, the most commonly observed adverse events with VERQUVO vs placebo, occurring at a frequency greater than or equal to 5%, were hypotension (16% vs 15%) and anemia (10% vs 7%).

There are no data on the presence of VERQUVO in human milk, the effects on the breastfed infant, or effects on milk production. Because of the potential for serious adverse reactions in breastfed infants from VERQUVO, advise women not to breastfeed during treatment with VERQUVO.

Concomitant use of VERQUVO with PDE-5 inhibitors is not recommended because of the potential for hypotension.

About the Worldwide Collaboration Between Bayer and Merck

Since October 2014, Bayer and Merck (known as MSD outside of the United States and Canada) have pursued a worldwide collaboration in the field of sGC modulators. The collaboration brings together two leading companies that have stated their intent to fully evaluate this therapeutic class in areas of unmet medical need. The vericiguat program is being co-developed by Bayer and Merck. Merck has the commercial rights to vericiguat in the U.S. and Bayer has the exclusive commercial rights in the rest of world. The companies share equally the costs of the development of vericiguat.

About Heart Failure with Reduced Ejection Fraction

Heart failure with reduced ejection fraction (HFrEF), formerly known as systolic heart failure, is characterized by the compromised ability of the heart to pump blood sufficiently during its contraction phase. In the U.S., approximately 6.2 million adults (20 years of age and older) have heart failure, and approximately 50% of heart failure patients have HFrEF. An observational, cohort analysis of PINNACLE registry data showed that approximately half of patients with worsening chronic HFrEF are rehospitalized within 30 days of a worsening event, and an estimated one in five patients with worsening chronic HFrEF will die within two years.

About Merck

For more than 125 years, Merck, known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases in pursuit of our mission to save and improve lives. We demonstrate our commitment to patients and population health by increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues

to be at the forefront of research to prevent and treat diseases that threaten people and animals – including cancer, infectious diseases such as HIV and Ebola, and emerging animal diseases – as we aspire to be the premier research-intensive biopharmaceutical company in the world. For more information, visit www.merck.com and connect with us on [Twitter](#), [Facebook](#), [Instagram](#), [YouTube](#) and [LinkedIn](#).

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company’s management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of the global outbreak of novel coronavirus disease (COVID-19); the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company’s 2019 Annual Report on Form 10-K and the company’s other filings with the Securities and Exchange Commission (SEC) available at the SEC’s Internet site (www.sec.gov).

Please see Prescribing Information, including Boxed Warning, for VERQUVO (vericiguat) at https://www.merck.com/product/usa/pi_circulars/v/verquvo/verquvo_pi.pdf and Medication Guide at https://www.merck.com/product/usa/pi_circulars/v/verquvo/verquvo_mg.pdf.

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