Verquvo™ (vericiguat)

Policy # 00752
Original Effective Date: 08/09/2021
Current Effective Date: 08/14/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Verquvo™‡ (vericiguat) to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility will be considered for Verquvo (vericiguat) when the following criteria are met:

- Patient has a diagnosis of symptomatic chronic heart failure (NYHA [New York Heart Association] Class II-IV); AND
- Patient's ejection fraction (EF) is less than 45%; AND
- Patient is 18 years of age or older; AND
- Patient has been hospitalized for heart failure in the past 6 months OR has required outpatient intravenous (IV) diuretics in the past 3 months; AND
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility based on clinical trials and will be denied as not medically necessary** if not met)*
- Patient has tried and failed (e.g., intolerance or inadequate response) therapy with Entresto®‡ (sacubitril/valsartan) unless there is clinical evidence or patient history that suggests the use of Entresto (sacubitril/valsartan) will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has tried and failed (e.g., intolerance or inadequate response) therapy with an ACE (angiotensin converting enzyme) inhibitor OR an ARB (angiotensin receptor blocker, not including Entresto [sacubitril/valsartan]) unless there is clinical evidence or patient history

that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

- Patient has tried and failed (e.g., intolerance or inadequate response) therapy with a beta blocker indicated for the treatment of heart failure (i.e., bisoprolol, carvedilol, metoprolol succinate) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient.
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Verquvo (vericiguat) when the patient has NOT been hospitalized for heart failure in the past 6 months OR when the patient has NOT required outpatient intravenous (IV) diuretics in the past 3 months to be **not medically necessary.****

Based on review of available data, the Company considers the use of Verquvo (vericiguat) when the patient has NOT tried and failed the pre-requisite medications for heart failure in the patient selection criteria to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Verquvo (vericiguat) when the patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

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Background/Overview

Verquvo is a soluble guanylate cyclase (sGC) stimulator, indicated to reduce the risk of cardiovascular death and heart failure (HF) hospitalization following a hospitalization for heart failure or need for outpatient IV diuretics, in adults with symptomatic chronic HF and ejection fraction less than 45%. Verquvo is available in 2.5 mg, 5 mg, and 10 mg tablets. The dosing is up-titrated to a targeted maintenance dose of 10 mg once daily.

Verquvo 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, Verquvo augments levels of intracellular cGMP, leading to smooth muscle relaxation and vasodilation.

Heart failure is due to the ability of the ventricle to fill with or eject blood. Heart failure has typically been classified into 3 categories: HF with preserved ejection fraction (LVEF [left ventricular ejection fraction] ≥50%), HR with midrange ejection fraction (LVEF 41%-49%), and HF with reduced ejection fraction (LVEF ≤40%). The reduced ejection fraction variety of HF is known as HFrEF. The goal of therapy in patients with HFrEF is to reduce morbidity and mortality. Verquvo is currently not addressed in heart failure treatment guidelines. The American College of Cardiology published a focused update in 2021 for the management of heart failure. The update noted that patients with HFrEF, therapy should include an ACE-inhibitor, ARB, or an ARNI (angiotensin receptor-neprilysin inhibitor), such as Entresto (preferred), and an evidence-based beta blocker (i.e. bisoprolol, carvedilol, metoprolol succinate). Once these medications are included in the HF treatment regimen, other medications classes are typically added on.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Verquvo is a soluble guanylate cyclase (sGC) stimulator, indicated to reduce the risk of cardiovascular death and heart failure (HF) hospitalization following a hospitalization for heart failure or need for outpatient IV diuretics, in adults with symptomatic chronic HF and ejection fraction less than 45%

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The purpose of this policy is to ensure usage of this medication in accordance with the FDA approved indication as well as in accordance with national guidelines.

VICTORIA was a randomized, parallel-group, placebo-controlled, double-blind, event-driven, multi-center trial comparing Verquvo and placebo in 5,050 adult patients with symptomatic chronic heart failure (NYHA class II-IV) and LVEF less than 45% following a worsening heart failure event. A worsening heart failure event was defined as heart failure hospitalization within 6 months before randomization or use of outpatient IV diuretics for heart failure within 3 months before randomization.

Patients were randomized to receive Verquvo 10 mg or matching placebo. Verquvo was initiated at 2.5 mg once daily and increased at approximately 2 week intervals to 5 mg once daily and the target dose of 10 mg once daily, as tolerated. Placebo doses were similarly adjusted. After approximately 1 year, 90% of patients in both treatment groups were treated with the 10 mg target dose.

The primary endpoint was a composite of time to first event of CV (cardiovascular) death or hospitalization for heart failure. The median follow-up for the primary endpoint was 11 months. 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%. Sixty-seven percent of the patients were enrolled within 3 months of a HF-hospitalization index event; 17% were enrolled within 3 to 6 months of HF hospitalization, and 16% were enrolled within 3 months of outpatient treatment with IV diuretics for worsening HF. At baseline, 93% of patients were on a beta blocker, 73% of patients were on an ACE inhibitor or ARB, 70% of patients were on a mineralocorticoid receptor antagonist (MRA), 15% of patients were on an ARNI, 28% of patients had an implantable cardiac defibrillator, and 15% had a biventricular pacemaker. Ninety-one percent of patients were treated with 2 or more heart failure medications (beta blocker, any renin-angiotensin system [RAS] inhibitor or MRA) and 60% of

patients were treated with all 3. At baseline, 6% of patients were on ivabradine and 3% of patients were on a sodium glucose co-transporter 2 (SGLT2) inhibitor.

In VICTORIA, Verquvo was superior to placebo in reducing the risk of CV death or heart failure hospitalization 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% annualized absolute risk reduction (ARR) with Verquvo compared with placebo. The treatment effect reflected a reduction in both cardiovascular death and heart failure hospitalization.

References

1. Verquvo [package insert]. Merck. Whitehouse Station, New Jersey. Updated January 2021.
2. Overview of the treatment of heart failure with reduced ejection fraction. UpToDate. Accessed June 2021.
3. Verquvo Drug Evaluation. Express Scripts. Updated January 2021.

Policy History

Original Effective Date: 08/09/2021
Current Effective Date: 08/14/2023

07/01/2021	Medical Policy Committee review
07/14/2021	Medical Policy Implementation Committee approval. New policy.
07/07/2022	Medical Policy Committee review
07/13/2022	Medical Policy Implementation Committee approval. No change to coverage.
07/06/2023	Medical Policy Committee review
07/12/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 07/2024

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and

whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.