Verquvo (vericiguat) Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date 09-01-2024

Date of Origin

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Verquvo® (vericiguat) Tablets	Reduce the risk of cardiovascular death and heart failure (HF) hospitalization following a hospitalization for HF or need for outpatient IV diuretics, in adults with symptomatic chronic HF and ejection fraction less than 45%		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Heart Failure

Heart failure (HF) is a complex clinical syndrome with symptoms and signs that result from any structural or functional impairment of ventricular filling or ejection of blood. The American Heart Association/American College of Cardiology (AHA/ACC) stages of heart failure emphasize the development and progression of disease, and advanced stages and progression are associated with reduced survival. The New York Heart Association (NYHA) classification is used to characterize symptoms and functional capacity of patients with symptomatic (NYHA Class II-IV) HF or advanced HF. In HF, NYHA functional class I includes patients with no limitations in physical activity resulting from their HF. NYHA class II includes patients who are comfortable at rest but have slight symptoms resulting from HF (dyspnea, fatigue, lightheadedness) with ordinary activity. NYHA class III includes patients who are comfortable at rest but have symptoms of HF with less than ordinary activity. NYHA class IV includes patients who are unable to carry out any physical activity without symptoms and have symptoms at rest. It is a subjective assessment by a clinician and can change over time. Although reproducibility and validity can be limited, the NYHA functional classification is an independent predictor of mortality, and it is widely used in clinical practice to determine the eligibility of patients for treatment strategies. Because of the complexity of HF management and coordination of other health and social services required, HF care is ideally provided by multidisciplinary teams that include cardiologists, nurses, and pharmacists who specialize in HF as well as dieticians, mental health clinicians, social workers, primary care clinicians, and additional specialists.(2)

Left ventricular ejection fraction (LVEF) is considered important in the classification of patients with HF because of differing prognosis and response to treatments and because most clinical trials select patients based on ejection fraction (EF). The classification of HF by LVEF is as follows:(2)

Type of HF According to LVEF	LVEF Criteria
HFrEF (HF with reduced EF)	Less than or equal to 40%

HFimpEF (HF with improved EF)	Previous LVEF less than or equal to 40% and a follow-up measurement of LVEF >40%
HFmrEF (HF with mildly reduced EF)	41-49% Evidence of spontaneous or provokable increased LV filling pressures
HFpEF (HF with preserved EF)	Greater than or equal to 50% Evidence of spontaneous or provokable increased LV filling pressures

Medication recommendations for HFmrEF (LVEF 41-49%) give a class of recommendation (COR) of 1 (strong) to diuretics, as needed followed by a COR of 2a (moderate) to sodium-glucose cotransporter 2 inhibitor (SGLT2i). EMPEROR-Preserved trial showed a significant benefit of empagliflozin in patients with symptomatic HF with LVEF >40%. There are no prospective randomized controlled trials for patients specifically with HFmrEF (LVEF, 41%–49%). All data for HFmrEF are from post hoc or subsets of analyses from previous HF trials with patients now classified as HFmrEF. LVEF is a spectrum, and among patients with LVEF 41% to 49%, patients with LVEF on the lower end of this spectrum appear to respond to medical therapies similarly to patients with HFrEF. Thus, it may be reasonable to treat these patients with guideline-directed medical therapy (GDMT) used for treatment of HFrEF (beta blockers; mineralocorticoid receptor antagonist [MRA]; angiotensin receptor-neprilysin inhibitor [ARNi], angiotensin-converting enzyme inhibitor [ACEi], or angiotensin receptor blocker [ARB]). A COR of 2b (weak) is assigned to these medications which are also used for HFrEF (beta blockers, MRA, ARNi, ACEi, ARB).(2)

Efficacy

Vericiguat is a stimulator of soluble guanylate cyclase (sGC), an 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, both independently and synergistically with NO, vericiguat increases levels of intracellular cGMP, leading to smooth muscle relaxation and vasodilation. Vericiguat also demonstrated a dose-dependent reduction in N-terminal-prohormone B natriuretic peptide (NT-proBNP), a biomarker in heart failure.(1)

Verquvo gained FDA approval through the VICTORIA trial. This was a randomized, parallel-group, placebo-controlled, double-blind, multicenter trial that enrolled 5,050 adult patients with symptomatic chronic heart failure (New York Heart Association class II-IV) that also had a left ventricular ejection fraction (LVEF) of less than 45%, following a worsening heart failure event. A worsening heart failure event was defined as a heart failure hospitalization within 6 months before randomization or use of outpatient intravenous diuretics for heart failure within 3 months before randomization. At baseline, 93% of patients were on a beta blocker, 73% of patients were on an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB), 70% of patients were on a mineralocorticoid receptor antagonist (MRA), 15% of patients were on a combination of an angiotensin receptor and neprilysin inhibitor (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. Patients in both the study drug and the placebo group had their doses titrated up as tolerated. The primary endpoint was a composite of time to first event of CV death or hospitalization for heart failure. The median follow-up for the primary endpoint was 11 months. Verquvo was found to be superior to placebo in reducing the risk of CV death or heart failure hospitalization based on a time-to-event analysis. Over the course of the study, there was a 4.2% annualized absolute risk reduction in CV death or heart failure hospitalization compared with placebo.(1)

Safety	Verquvo is contraindicated in patients with concomitant use of other soluble guanylate cyclase (sGC) stimulators and in patients that are pregnant.(1) Verquvo has a boxed warning for embryo-fetal toxicity.(1) • Do not administer VERQUVO to a pregnant female because it may cause fetal harm. • 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.

REFERENCES

Number	Reference
1	Verquvo prescribing information. Merck Sharp & Dohme LLC. July 2023.
2	Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145(18). doi:10.1161/cir.0000000000001063

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Verquvo	vericiguat tab	10 MG ; 2.5 MG ; 5 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Verquvo	vericiguat tab	10 MG ; 2.5 MG ; 5 MG	30	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Verquvo	vericiguat tab	10 MG ; 2.5 MG ; 5 MG	Commercial ; HIM ; ResultsRx

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PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All target agents are eligible for continuation of therapy 1. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** B. The patient has a diagnosis of symptomatic chronic heart failure (NYHA Class II-IV) and ALL of the following: 1. The patient has a left ventricular ejection fraction (LVEF) less than 45% **AND** 2. ONE of the following: A. Hospitalization of heart failure within the past 6 months **OR** B. Use of outpatient IV diuretics for heart failure within the past 3 months **OR** C. The patient has another FDA labeled indication for the requested agent and route of administration **OR** D. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., cardiologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS or DrugDex 1 or 2a level of evidence NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria. **Length of Approval:** 12 months **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., cardiologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**

Module	Clinical Criteria for Approval
	4. The patient does NOT have any FDA labeled contraindications to the requested agent NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria. **Length of Approval:** 12 months

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Universal QL	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following: A. BOTH of the following: 1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **OR** B. BOTH of the following: 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 2. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** C. BOTH of the following: 1. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **Length of Approval**: up to 12 months