STEPS

New Drug Reviews

Vericiguat (Verquvo) for the Treatment of Heart Failure

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Drug	Dosage	Dose form	Cost of full course*
Vericiguat (Verquvo)	Initial dosage of 2.5 mg once daily with food, then doubled every two weeks to reach target dosage of 10 mg daily, as tolerated	Tablets: 2.5 mg; 5 mg; 10 mg	$640

*—Estimated lowest GoodRx price for one month of treatment. Actual cost will vary with insurance and by region. Information obtained at https://www.goodrx.com (accessed September 6, 2022; zip code: 66211).

Vericiguat (Verquvo) is labeled for the treatment of adults with symptomatic chronic heart failure (HF) and an ejection fraction of less than 45%. It is used to reduce the composite risk of cardiovascular death and HF-related hospitalization following a previous hospitalization for HF or the need for outpatient intravenous diuretics.[1] Vericiguat causes smooth muscle relaxation and vasodilation by stimulating soluble guanylate cyclase (which is decreased in HF), both independently and synergistically with nitric oxide, a unique mechanism.

Safety

In a study involving 2,519 patients, approximately 16% experienced symptomatic hypotension or syncope. Systolic blood pressure may decrease slightly within the first 16 weeks of treatment but can return to baseline.[2] In clinical trials, anemia occurred more often in the vericiguat group than in the placebo group (7.6% vs. 5.7%), and 1.6% of the anemia cases in the vericiguat group were considered serious adverse events. The average change in hemoglobin level from baseline to 16 weeks was −0.38 g per dL in the vericiguat group and −0.14 g per dL in the placebo group.

No dosing adjustments are required in patients with an estimated glomerular filtration rate of 15 mL per minute per 1.73 m^2 or more, or mild to moderate hepatic impairment. Vericiguat has not been studied in patients with end-stage renal disease, dialysis, or severe hepatic impairment. Vericiguat may cause fetal harm and should not be used in patients who are pregnant or breastfeeding. Vericiguat has not been studied in children.[1]

Tolerability

Patients taking vericiguat may have increased rates of symptomatic hypotension and should monitor their blood pressure regularly, especially following dose titrations. Patients also taking long-acting nitrates may be at increased risk of hypotension, although clinically significant differences have not been shown in drug interaction studies. Concomitant use with sildenafil (Viagra) is associated with a reduction in seated blood pressure of approximately 5.4 mm Hg. Because of the limited study, concomitant use with phosphodiesterase inhibitors is not recommended. Vericiguat should not be given to patients receiving riociguat (Adempas).

Effectiveness

The effectiveness of vericiguat was evaluated in a single study of 5,050 patients with New York Heart Association class II to IV HF, an ejection

STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

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fraction of less than 45%, and evidence of worsening HF (i.e., hospitalized within six months or receiving intravenous diuretic therapy in the outpatient setting within the previous three months). All patients were also treated with usual HF treatments, with a majority (60%) receiving triple therapy (i.e., a beta blocker; a mineralocorticoid receptor antagonist; and an angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, or angiotensin receptor–neprilysin inhibitor). The primary outcome was a composite of death from cardiovascular causes or first hospitalization for HF; it occurred in fewer patients in the vericiguat group vs. the placebo group based on a time-to-event analysis (number needed to treat = 34 for 11 months; 95% CI, 18 to 169).[1] However, the rates of first HF hospitalization, overall mortality, and cardiovascular mortality were not individually decreased with treatment. There were fewer total (first and recurrent) HF hospitalizations in the treated group (number needed to treat = 34 for 11 months; 95% CI, 19 to 314). Using the Kansas City Cardiomyopathy Questionnaire, this study also determined that vericiguat showed quality of life improvement similar to placebo.[3]

Vericiguat has not been adequately studied in patients taking sodium-glucose cotransporter-2 (SGLT-2) inhibitors or ivabradine (Corlanor). There is no evidence comparing vericiguat to SGLT-2 inhibitors or ivabradine as an add-on to triple therapy.

Price

Vericiguat costs about $640 per month, in addition to other HF treatments. This cost is similar to other brand name add-on HF treatment options. However, many insurance formularies list vericiguat as a higher-tier medication and may require prior authorization or higher monthly copays.

Simplicity

The recommended starting dosage of vericiguat is 2.5 mg by mouth once daily with food. The dosage is then doubled every two weeks to the target maintenance dosage of 10 mg once daily, as tolerated. Tablets may be crushed and mixed with water for patients who have difficulty swallowing them.

Bottom Line

In patients with symptomatic HF with reduced ejection fraction following hospitalization for HF or the need for outpatient intravenous diuretics, the impact of vericiguat as an add-on treatment to optimal triple therapy on the composite of risk of death from cardiovascular causes and HF hospitalization is small. It has not been shown to have an effect on overall mortality, cardiovascular mortality, or quality of life. Given the substantial benefits of SGLT-2 inhibitors in recent trials, including a reduction in all-cause and cardiovascular mortality, and the addition of SGLT-2 inhibitors to initial therapy in current guideline recommendations, vericiguat should be reserved for select patients with HF who are symptomatic despite optimal four-drug guideline-directed medical therapy that includes a beta blocker, a mineralocorticoid receptor antagonist, an angiotensin receptor–neprilysin inhibitor, and an SGLT-2 inhibitor.[4] Accessibility issues due to cost and insurance coverage may limit the use of vericiguat.

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