NEW DRUGS

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Vericiguat

Approved indication: add-on to standard therapy for adults with symptomatic chronic heart failure with reduced ejection fraction (less than 45%) stabilised after a recent heart failure decompensation event requiring hospitalisation or intravenous diuretic therapy

Verquvo (Bayer)
2.5 mg, 5 mg and 10 mg film-coated tablets

Vericiguat is used in the specialist management of chronic heart failure with reduced ejection fraction (HFrEF). It stimulates the enzyme soluble guanylate cyclase (sGC), which amplifies the normal vasorelaxant effects of nitric oxide.[1] Another sGC stimulator, riociguat, has been approved in Australia for many years for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension.[2]

Vericiguat is approved as an add-on to standard therapy for adults with symptomatic chronic HFrEF (ejection fraction less than 45%) who have been stabilised after a recent decompensation event that required hospitalisation or intravenous diuretic therapy.[2]

Standard treatment for people with HFrEF involves combination therapy with the following 4 drug classes:

- renin–angiotensin system inhibitors (such as angiotensin-receptor neprilysin inhibitors or angiotensin converting enzyme inhibitors or angiotensin II receptor blockers)
- heart failure–specific beta blockers
- mineralocorticoid receptor antagonists
- sodium-glucose co-transporter 2 inhibitors.[3]

A 2022 Australian guidance update for heart failure recommends vericiguat can be added as a fifth drug for people with persistent HFrEF (ejection fraction 40% or less and ongoing symptoms or signs or limited functional capacity) with a history of recent hospitalisation and at high risk of readmission.[4]

The pivotal study supporting vericiguat's registration by the Therapeutic Goods Administration (TGA) was the 2020 phase 3 randomised, double-blind, placebo-controlled VICTORIA study involving 5050 people.[5] Vericiguat (starting dose 2.5 mg orally, daily, titrated up to 10 mg orally, daily) was added to standard treatment in 2526 people with chronic heart failure (New York Heart Association class II to IV) and an ejection fraction less than 45% with evidence of worsening heart failure. The primary outcome was a composite of death from cardiovascular causes or first hospitalisation for heart failure. Patients in the vericiguat group experienced a 10% risk reduction compared with placebo for the primary outcome, with an absolute risk reduction of 3% over a median follow-up of 10.8 months.[5] The number needed to treat with vericiguat for one year to prevent a primary outcome event was 24.[5]

People older than 65 years experienced less benefit from vericiguat compared with younger people.[5] There continues to be uncertainty about the drug's utility in older people.

A 2021 analysis of prespecified subgroups in the VICTORIA study found those who were hospitalised for HFrEF recently (within 3 months of an index hospitalisation) were more vulnerable to death or recurrent hospitalisation, irrespective of treatment with vericiguat.[6] The shorter the interval from hospitalisation, the higher the risk. It concluded that people on vericiguat for HFrEF who recently experienced a worsening heart failure event retained high residual risk for hospitalisation and death.

A 2023 meta-analysis of 4 randomised, placebo-controlled trials (6705 patients, including the VICTORIA study) combined patients with both preserved and reduced ejection fraction chronic heart failure, to assess the efficacy of vericiguat. While the study found no statistically significant difference in rates of cardiovascular death and hospitalisation for heart failure, there was a trend towards fewer deaths and hospitalisations in patients with an ejection fraction less than 45%. It suggested more clinical trials were required to verify vericiguat's efficacy.[7]

The most common adverse effects of vericiguat are cardiovascular (e.g. hypotension, syncope), haematological (e.g. anaemia of unknown cause, iron deficiency anaemia) and gastrointestinal (e.g. nausea, dyspepsia).[5] Hypotension may be accentuated by vericiguat in people on other vasodilators (e.g. isosorbide dinitrate, sildenafil). Vericiguat is contraindicated in people taking riociguat.

Vericiguat may induce the cytochrome P450 enzyme CYP3A4, potentially affecting the metabolism of many drugs, but more study is required to confirm this.

Vericiguat is available in a range of tablet strengths to be taken orally with food. The recommended starting dose is 2.5 mg once daily; the dose should be doubled approximately every 2 weeks to a maintenance dose of 10 mg once daily, as tolerated. Vericiguat is absorbed within 1 to 2 hours, is 98% plasma-protein bound, and metabolised in the liver to an inactive metabolite. In mild to moderate liver or kidney disease, dose adjustment is not necessary; however, because of lack of data, people with severe liver or kidney impairment should avoid vericiguat.

There are no human data about the use of vericiguat in pregnancy and breastfeeding.

In summary, vericiguat is a relatively new addition to the armamentarium of drugs for people with HFrEF. Most of the information on its safety and efficacy comes from the 2020 VICTORIA study[5] that resulted in its TGA approval; however, a 2023 meta-analysis of various studies gives a more guarded interpretation of benefit.[7]

T T manufacturer provided additional useful information. The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.

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