NEW DRUGS

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Finerenone

Approved indication: chronic kidney disease associated with type 2 diabetes with albuminuria

Kerendia (Bayer)

10 mg and 20 mg film-coated tablets

Diabetes is a leading cause of chronic kidney disease. Both diabetes and diabetic kidney disease increase the risk of cardiovascular disease. Slowing the progression of chronic kidney disease and addressing cardiovascular disease risk are important components of diabetes management.[1]

Overactivation of mineralocorticoid receptors has been implicated in cardiorenal diseases. Steroidal mineralocorticoid-receptor antagonists (MRAs), such as spironolactone, may preserve kidney function, but are associated with increased risk of hyperkalaemia.[2,3] Finerenone is a novel nonsteroidal MRA that is associated with a lower risk of hyperkalaemia than steroidal MRAs.

Finerenone's approved indication is to delay progressive decline of kidney function in adults with chronic kidney disease (with albuminuria) associated with type 2 diabetes who are already taking the maximum tolerated dose of an angiotensin converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB).

Two randomised controlled trials—FIDELIO-DKD[4] and FIGARO-DKD[5]—compared finerenone to placebo in adults with type 2 diabetes and diabetic kidney disease. Patients had persistent, moderate or severe albuminuria and were receiving a maximum tolerated dose of ACEI or ARB therapy. A pre-specified pooled analysis of individual patient data from these trials (FIDELITY) reported outcomes for 13,026 patients across a broad spectrum of chronic kidney disease with a median follow-up of 3 years.[6] Key study end points were composite kidney and cardiovascular outcomes.* The composite kidney outcome occurred in 360 (5.5%) patients receiving finerenone and 465 (7.1%) receiving placebo (hazard ratio [HR] 0.77; 95% confidence interval [CI] 0.67–0.88). The composite cardiovascular outcome occurred in 825 (12.7%) patients receiving finerenone and 939 (14.4%) receiving placebo (HR 0.86; 95% CI 0.78–0.90).

About 14% of patients were receiving a sodium-glucose co-transporter 2 (SGLT2) inhibitor or a glucagon-like peptide-1 (GLP-1) receptor agonist at the start of the trial.[6] As these drugs also have kidney and cardiovascular benefits and are used as part of the management of diabetic nephropathy, subgroup analyses were conducted to explore the effect of finerenone in patients with and without these drugs. These analyses suggest the kidney and cardiovascular benefits of finerenone are observed regardless of the use of SGLT2 inhibitors or GLP-1 receptor agonists;[7,8] however, further studies are needed to understand the potential benefits and harms of these combinations.

The most common adverse effect of finerenone was hyperkalaemia, which occurred in 14.0% of patients in the finerenone group compared with 6.9% in the placebo group. Hospitalisation for hyperkalaemia occurred in 0.9% of the finerenone-treated patients and 0.2% of the placebo-treated patients, and permanent treatment discontinuation due to hyperkalaemia occurred in 1.7% and 0.6% of patients respectively.[6] Other less common adverse effects were hypotension, hyponatraemia and initial decline of estimated glomerular filtration rate (eGFR). The frequency of gynaecomastia was low, and similar to placebo.[5]

Serum potassium concentration and eGFR should be measured before starting finerenone. If serum potassium concentration is more than 5.0 mmol/L, or eGFR is less than 25 mL/min/1.73 m^2, starting finerenone is not recommended.

The recommended initial finerenone dose is 20 mg orally daily. In people with an eGFR less than 60 mL/min/1.73 m^2 but greater than or equal to 25 mL/min/1.73 m^2, the starting dose is reduced to 10 mg orally daily.

Serum potassium concentration and eGFR should be repeated 4 weeks after starting or increasing the dose of finerenone. The product information provides details for dose adjustment based on serum potassium concentration and eGFR. Once treatment is established, serum potassium concentration should be remeasured periodically, and finerenone withheld if serum potassium concentration exceeds 5.5 mmol/L.

Concomitant use of finerenone with potassium-sparing diuretics should be avoided. When used with trimethoprim, temporary discontinuation of finerenone may be required, or serum potassium concentrations monitored.

Finerenone is almost completely metabolised to inactive compounds by cytochrome P450 (CYP) 3A4 and, to a lesser extent, by CYP2C8. Finerenone

* Composite kidney outcome: time to first onset of kidney failure, a decrease in estimated glomerular filtration rate from baseline of at least 57% for a period of at least 4 weeks, or death from renal causes. Composite cardiovascular outcome: time to cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or hospitalisation for heart failure.

should be avoided in patients with severe hepatic impairment. Coadministration with strong CYP3A4 inhibitors (eg itraconazole, clarithromycin) is contraindicated. Co-administration with grapefruit or grapefruit juice should also be avoided.

Finerenone is Therapeutic Goods Administration pregnancy Category D. Adverse effects on embryofetal development, including teratogenicity, were observed in animals, but there are no human data.

Finerenone provides an additional treatment option to delay progressive decline of kidney function in people with type 2 diabetes and moderate-to-severe albuminuria who are already receiving an optimal dose of an ACEI or ARB, with or without the use of an SGLT2 inhibitor or GLP-1 receptor agonist.

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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