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Finerenone for Heart Failure with Mildly Reduced or Preserved Ejection Fraction

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Introduction: Patients with heart failure with mildly reduced ejection fraction (HFmrEF) have a left ventricular ejection fraction (LVEF) of 41-49%, while those with preserved ejection fraction heart failure (HFpEF) possess a LVEF ≥ 50%.[1] These forms of heart failure are more common in older adults and are frequently associated with comorbidities such as hypertension and diabetes.[1,2] Steroidal mineralocorticoid receptor antagonists (MRAs) (e.g., spironolactone or eplerenone) reduce disease burden and mortality in patients with heart failure and reduced ejection fraction. However, their benefit in individuals with mildly reduced or preserved ejection fraction remains unclear.[3-5] Finerenone (Kerendia®) is a nonsteroidal mineralocorticoid receptor blocker that has physiochemical properties distinct from spironolactone or eplerenone. It was approved by the Food and Drug Administration (FDA) to reduce the risk of cardiovascular (CV) death, hospitalization for heart failure (HF), and urgent HF visits in adult patients with LVEF ≥ 40% in July 2025.[4-6]

Mechanism of Action: Finerenone is a highly potent non-steroidal MRA that specifically blocks mineralocorticoid receptor-mediated sodium reabsorption and overactivation in the epithelial (e.g., kidney) and nonepithelial (e.g. blood vessels, heart) tissues, decreasing inflammation and fibrosis.[3] Approximately 90% of this medication is converted via hepatic Cytochrome P450 3A4 (CYP3A4) to inactive metabolites.

Clinical Trial: The Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction (FINEARTS-HF) trial was a double-blind, randomized, placebo-controlled study that evaluated the use of finerenone in patients with HFmrEF and HFpEF.[5] The study included a total of 6001 patients who met these eligibility requirements: ≥40 years old with New York Heart Association (NYHA) class II-IV symptomatic HF, LVEF ≥40%, structural heart disease, and elevated natriuretic peptides. All patients had an estimated glomerular filtration rate (eGFR) ≥25 mL/min/1.73m^2, serum potassium ≤5.0 mEq/L, and were receiving standard therapy. Participants were randomized 1:1 to finerenone (n=3003) or placebo (n=2998). The trial's median duration was 2.7 years. The dose of finerenone was titrated toward a maximum of 20–40 mg daily based on the baseline eGFR. The primary endpoint was a composite of CV death and total HF events (first and recurrent hospitalizations or urgent visits). Secondary endpoints included reduction in the total number of worsening HF events, improvement in NYHA class at 12 months, kidney composite outcome events (≥ 50% decline in eGFR, progression to <15 mL/min/1.73m^2, or need for dialysis or kidney transplant), death from any cause, and change from baseline in the total symptom score on the Kansas City Cardiomyopathy Questionnaire (KCCQ) at 6, 9, and 12 months. Adverse events were also assessed. The

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finerenone group had a significantly lower risk of the primary composite endpoint than the placebo group (RR 0.84; 95% CI 0.74–0.95; p=0.007). The results of the primary composite endpoint were driven by the reduction in total HF events (RR 0.82; 95% CI, 0.71-0.94; p=0.006)) since deaths from CV causes between groups were not significantly different (RR 0.93; 95% CI 0.78-1.11). For the secondary endpoints, there was no meaningful difference in improvement in NYHA functional class at 12 months (OR 1.01, 95% CI, 0.88–1.15). The kidney composite outcome did not favor finerenone (HR 1.33; 95% CI, 0.94–1.89). Worsening renal events were more frequent with finerenone than placebo, including renal impairment (7% vs 4%, respectively), decreased eGFR (5% vs 4%, respectively), acute kidney injury (4% vs 2%, respectively), and renal failure (3% vs 2%, respectively). The rate of death from any cause was not significantly different between groups (HR 0.93; 95% CI, 0.83–1.06). The least-square mean (± SE) change from baseline in the KCCQ total score estimated as total treatment effect over 6, 9, and 12 months was 8 ± 0.3 points in the finerenone group compared with 6.4 ± 0.3 in the placebo group (difference, 1.6 points, 95% CI, 0.8-2.3; p<0.001). The authors concluded that in individuals with HFmrEF or HFpEF, finerenone was associated with a significantly reduced rate of total worsening HF events and death from CV causes and better patient-reported health status compared with placebo.

Safety: The most common adverse events occurring in ≥ 1% of patients receiving finerenone were hyperkalemia, hyponatremia, and hypotension.[3-5] Finerenone can cause worsening of renal function. Potassium levels and eGFR should assessed before initiation of therapy and should be carefully monitored after any dose adjustments.[3,4] Finerenone should be avoided in patients with severe hepatic impairment and additional serum potassium monitoring is recommended in those with moderate hepatic impairment (Child Pugh A or B). Initiation of finerenone in patients with an eGFR < 25 mL/min/1.73 m^2 is not recommended.

Drug Interactions: Strong CYP3A4 inhibitors are contraindicated with finerenone. Grapefruit or grapefruit juice should be avoided while taking this medication. Concurrent use of moderate or weak CYP3A4 inhibitors requires careful monitoring of serum potassium during drug initiation or dosage adjustments of either finerenone or the inhibitor. It is recommended to avoid concurrent use of strong or moderate CYP3A4 inducers with finerenone.

Dosing and Administration: Finerenone may be administered with or without food.[3] For those unable to swallow whole tablets, finerenone can be crushed and mixed with water or soft foods, such as applesauce, immediately before oral administration. Dosing for heart failure is based on eGFR and serum potassium level. The target daily dose is 40 mg orally once daily for patients with an eGFR ≥ 60 mL/min/1.73 m^2 at initiation, and 20 mg orally once daily for those with an eGFR between 25 and < 60 mL/min/1.73 m^2. Dosing of finerenone based on potassium levels is listed in the package insert.[4] Any missed doses of finerenone should be taken as soon as possible; however, if not taken on the same day, the dose should be omitted.[3]

Cost and Availability: Finerenone is available as a film-coated tablet in three strengths: 10 mg, 20 mg, and 40 mg (NDC: 50419-540-01, 50419-541-01, 50419-542-01, respectively).[4] All three strengths have an average wholesale price of $27.47 for each tablet.[3] The cost for a patient requiring 30 tablets per month would be about $824. Finerenone should be stored in its original container at controlled room temperature (20-25°C [68 to 77°F]) with permitted excursions between 15-30°C [59 to 86°F].[4]

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