Finerenone (KERENDIA) for Heart Failure with Preserved Ejection Fraction (HFpEF) and Mildly Reduced Ejection Fraction (HFmrEF)
National Drug Mini-monograph
November 2025

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION

Description / MOA	Finerenone is a nonsteroidal, selective mineralocorticoid receptor antagonist (MRA) with no relevant affinity for androgen, progesterone, estrogen, and glucocorticoid receptors.
Indication Under Review	▪ Patients with heart failure (HF) with left ventricular ejection fraction (LVEF) ≥40% to reduce the risk of cardiovascular (CV) death, HF hospitalization, and urgent HF visits ▪ *Of note, finerenone is also approved for use in patients with chronic kidney disease associated with type 2 diabetes (NOT included in this review).*
Dosage Regimen	▪ **Required baseline labs:** Serum potassium and estimated renal function (eGFR, in mL/min/1.73m^2) prior to initiation ▪ **Do not initiate finerenone:** if serum potassium is >5 mEq/L or eGFR <25 mL/min/1.73m^2) ▪ **Initial dose** is based on eGFR at the time of finerenone initiation: ○ 20 mg once daily eGFR ≥ 60 ○ 10 mg once daily eGFR 25 to <60 ○ Not recommended for eGFR <25 ▪ Dose adjustments are made at 4 weeks based on serum potassium level and the initial eGFR (mL/min/1.73m^2). ▪ **Target dose:** ○ 40 mg once daily for patients with initial eGFR ≥60 ○ 20 mg once daily for patients with initial eGFR ≥25 to <60 ▪ **Follow-up labs:** Monitor serum potassium at 4 weeks after starting treatment and periodically thereafter; monitor eGFR periodically.
Dosage Forms Under Review	Oral tablet, film coated; 10 mg, 20 mg, 40 mg

EFFICACY CONSIDERATIONS

Trial/Design	**FINEARTS-HF:** International, event-driven, double-blind, randomized, placebo-controlled trial in patients with symptomatic HF and LVEF ≥40% ▪ **Primary endpoint:** Composite of total worsening HF events (defined as unplanned urgent care visit or hospitalization for HF) and cardiovascular death
Population	▪ **Key inclusion criteria:** ≥40 yrs old, symptomatic HF, LVEF ≥40%, structural heart disease, and elevated natriuretic peptides ▪ **Key exclusion criteria:** eGFR <25 mL/min/1.73m^2, serum potassium >5 mmol/L ▪ **N** = 6,001; **Median follow-up duration:** 32 months ▪ **Baseline demographics** (mean): 72 yrs old; 46% female; 79% White; 1% Black; 21% North America; eGFR 62 mL/min/1.73m^2; 69% NHYA functional class II; 13% SGLT-2i
Intervention	Finerenone target dose of 20 or 40 mg daily (dosing per baseline eGFR) vs. placebo (1:1)

Results

Primary Endpoint	Finerenone (n=3,003)	Placebo (n=2,998)	Rate ratio
1^o composite: Total worsening HF events and CV death* (# of events, # of events per 100 pt-yr)	1,083 (14.9)	1,283 (17.7)	0.84 (0.74-0.95)
Worsening HF events* (# of events)	842	1,024	0.82 (0.71-0.94)
CV death (# of patients)	242	260	0.93 (0.78-1.11)

*p <0.05; No improvement in NYHA functional class or all cause mortality; small improvement in KCCQ score not considered clinically significant

SAFETY CONSIDERATIONS

Boxed Warnings: None

Contraindications: Hypersensitivity, concomitant strong CYP3A4 inhibitors, adrenal insufficiency

Other Warnings

- Hyperkalemia
  - Increased risk with worsening renal function and in patients with higher baseline potassium levels or other risk factors for hyperkalemia
  - Measure serum potassium and eGFR before initiating finerenone and periodically during treatment (may require dose adjustment).
  - Do not initiate if potassium level >5 mEq/L.
- Worsening of renal function (in patients with HF)
  - Measure eGFR before initiating finerenone and periodically during treatment (may require dose adjustment).
  - Do not initiate if eGFR <25 mL/min/1.73m^2.

Table: Hyperkalemia and worsening renal function events from FINEARTS

Event	Finerenone N=2,993	Placebo N=2,993
Hyperkalemia		
Serum potassium level >5.5 mmol/L	14.3%	6.9%
Serum potassium level >6 mmol/L	3%	1.4%
Leading to hospitalization	0.5%	0.2%
Worsening renal function		
Any	18%	12%
Serum creatinine ≥3 mg/dL	2%	1.2%
Resulting in hospitalization	2%	1.3%
Hypokalemia	15.2%	26.2%

Top AEs: Hyperkalemia, worsening renal function

Pregnancy: No available data in pregnancy. Developmental toxicity in animals has been identified at 2 times the human dose; the clinical significance is unclear.

Lactation: No available data on human milk. Data suggest that finerenone is present in rat milk and is therefore likely present in human milk. Because of the potential risk to breastfed infants, avoid breastfeeding during treatment and for one day after treatment.

PLACE IN THERAPY

DRUG	FORMULARY STATUS	CLINICAL GUIDANCE	OTHER CONSIDERATIONS
Finerenone (KERENDIA)	Nonformulary, CFU ▪ HFpEF/mrEF ▪ CKD+T2DM	▪ FDA indicated for HF with LVEF ≥40%, CKD with T2DM ▪ Not yet specifically included in HF guidelines	▪ Nonsteroidal, selective MRA ▪ AEs: hyperkalemia, worsening renal function ▪ Contraindicated with concomitant strong CYP3A4 inhibitors
Spironolactone (ALDACTONE)	Formulary	▪ Off-label for HFpEF/HFmrEF ▪ FDA indicated for hypertension, HFrEF, primary aldosteronism, edema in cirrhosis and nephrotic syndrome ▪ **AHA/ACC/HFSA 2022 Guideline (2b recommendation):** MRAs may be considered in HFpEF to decrease hospitalizations and CV death in HFmrEF (LVEF 45-49%), particularly patients at the lower end of the LVEF spectrum	▪ Steroidal, nonselective MRA ▪ AEs: hyperkalemia, worsening renal function, gynecomastia, menstrual irregularities ▪ **Evidence summary: TOPCAT Trial -** Evaluated spironolactone vs. PBO in patients with HF and LVEF ≥45%. ○ **Overall Result**: No benefit found in the overall population ○ **Concerns**: Marked differences between patients in the Americas (~51% of participants) vs. Russia/Georgia. ○ **Americas Subgroup Findings**: Primary composite outcome (CV death, aborted cardiac arrest, HF hospitalization) reduced by **18%**. Spironolactone associated with higher risk of

				hyperkalemia (26% vs. 9% for K ≥5.5 mEq/L) and serum creatinine ≥3 mg/dL (9.8% vs. 9.1%). ○ **Regulatory and Guideline Impact**: Americas findings Led to **Class IIb recommendation** for MRAs (based on spironolactone) in HFpEF and HFmrEF in **2022 ACC/AHA HF Guidelines**. Of note, in 2020 the FDA Cardiovascular and Renal Drug Advisory Committee supported use of subgroup data for indication consideration.
	Eplerenone (INSPRA)	Formulary	▪ Off-label for HFpEF/HFmrEF and HF with reduced ejection fraction (HFrEF) ▪ FDA approved for hypertension, HFrEF post-myocardial infarction ▪ Not specifically mentioned in the AHA/ACC/HFSA 2022 Guideline	▪ Steroidal, selective MRA ▪ AEs: hyperkalemia, increased serum creatinine ▪ Limited data in HFpEF

VHA PLACE IN THERAPY	**Potential Use for HFpEF and HFmrEF in VHA**	▪ HFpEF is a heterogeneous clinical syndrome characterized by a normal or near-normal LVEF of 50% or higher. HFpEF accounts for approximately 50% of all HF and is associated with considerable morbidity and mortality. ▪ HFmrEF is defined as clinical HF with LVEF 41-49%. Patients with HFmrEF may have declining, improving, or stable LVEF. Evaluation of treatments in HFmrEF in clinical trials has mostly been conducted through post-hoc analyses or as subgroup analyses. ▪ Overall management of HFpEF includes risk stratification and management of comorbidities (e.g., hypertension, diabetes, obesity, CKD, AF, etc.); 2) nonpharmacologic strategies (e.g., weight management and exercise); 3) loop diuretics for symptom management; and 4) SGLT2i, MRAs, ARNIs and ARBs. ▪ ACC/AHA/HFSA 2022 HF guidelines provide strong recommendations in HFpEF for the use of loop diuretics for symptom management (class 1) and SGLT2 inhibitors to reduce HF hospitalizations and CV mortality (class 2a). MRAs, ARNIs, and ARBs may be considered (class 2b). ▪ The MRA recommendation in the ACC/AHA/HFSA 2022 HF guidelines is based on evidence of benefit with the use of spironolactone in patients with HF and LVEF ≥45% since the guidelines were published prior to the FINEARTS trial. ○ Spironolactone was evaluated in patients with HF and LVEF ≥45% in the placebo-controlled, international TOPCAT trial. Though the results in the overall trial were negative, a post-hoc regional Americas analysis found that spironolactone significantly reduced the composite primary endpoint of HF hospitalization and CV death. ▪ In the FINEARTS trial, finerenone reduced the composite primary endpoint of HF worsening events and CV death compared to placebo in patients with HF and LVEF of ≥40%. The benefit was driven by the reduction in HF worsening events. There was no improvement in CV death, all-cause death, or NYHA functional class. ▪ Despite exclusion of patients with a baseline potassium of >5 mmol/L and eGFR <25 mL/min/1.73 m^2, finerenone is associated with a 2-fold increased risk of hyperkalemia and a 2-fold increased risk of worsening renal function (SCr ≥3 mg/dL), though only a small number of patients required hospitalization for these AEs. Finerenone is associated with less hypokalemia compared to placebo. Baseline and follow-up monitoring of potassium and renal function are needed. ▪ As a nonsteroidal MRA, finerenone is not associated with gynecomastia or menstrual irregularities that can occur with steroidal MRAs (e.g., spironolactone). ▪ There are no head-to-head comparisons of finerenone and other MRAs including the formulary agent, spironolactone, in the management of HFpEF or HFmrEF. ▪ Ongoing manufacturer sponsored studies with finerenone in HFpEF/HFmrEF population include: 1) REDEFINE-HF evaluating patients with HF with LVEF ≥40% who are hospitalized for acute, decompensated HF (Apr 2026); and 2) CONFIRMATION-HF studying finerenone plus empagliflozin vs. usual care in patients with HF (all LVEF) (Aug 2026).

Abbreviations: ACC=American College of Cardiology; ACEI=angiotensin converting enzyme inhibitor; AEs=adverse events; AF=atrial fibrillation; AHA=American Heart Association; ARB=angiotensin receptor blocker; ARNi=angiotensin receptor-neprilysin inhibitor; CV=cardiovascular; eGFR=estimated glomerular filtration rate; HFSA=Heart Failure Society of America; KCCQ=Kansas City Cardiomyopathy Score; NYHA=New York Heart Association; MOA=mechanism of action; SGLT-2i=sodium-glucose cotransporter-2 inhibitor; T2DM=type 2 diabetes mellitus

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