Kerendia (finerenone)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Kerendia
- **Generic name:** Finerenone
- **Pharmacologic class:** Nonsteroidal mineralocorticoid receptor antagonist (MRA)
- **Strength and Formulation:** 10mg, 20mg; tablets
- **Manufacturer:** Bayer HealthCare Pharmaceuticals
- **How supplied:** Tabs—30, 90
- **Legal Classification:** Rx

Indication

- To reduce the risk of **sustained eGFR decline**, **end stage kidney disease**, **cardiovascular death**, **non-fatal myocardial infarction**, and **hospitalization for heart failure** in adults with chronic kidney disease associated with type 2 diabetes.

MPR

Dosage and Administration

- Swallow whole.
- If unable to swallow, tabs may be crushed and mixed with water or soft foods (eg, applesauce).
- Measure serum K^+ levels and estimated glomerular filtration rate (eGFR) prior to initiation.
- Do not initiate treatment if serum K^+ is >5.0mEq/L.
- Recommended starting dosage based on eGFR:
  - eGFR (≥60mL/min/1.73m^2): initially 20mg once daily.
  - eGFR (≥25 to <60mL/min/1.73m^2): initially 10mg once daily.
  - eGFR (<25mL/min/1.73m^2): not recommended.
- Target daily dose is 20mg.

MPR

Dosage and Administration

Monitoring and Dose Adjustment

- Measure serum K^+ 4 weeks after initiation, periodically during treatment, and adjust dose as needed.
- Dose adjustment based on current serum K^+ and current dose:

		Current Kerendia Dose	
		10mg once daily	**20mg once daily**
Current Serum Potassium (mEq/L)	**≤4.8**	Increase to 20mg once daily*	Maintain 20mg once daily
	>4.8–5.5	Maintain 10mg once daily	Maintain 20mg once daily
	>5.5	Withhold. Consider restarting at 10mg once daily when ≤5.0mEq/L.	Withhold. Restart at 10mg once daily when ≤5.0mEq/L.

*If eGFR has decreased by more than 30% compared to previous measurement, maintain 10mg dose.

MPR

Considerations for Specific Populations

- **Pregnancy:** No available data to evaluate drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.
- **Nursing mothers:** Avoid breastfeeding during and 1 day after treatment.
- **Pediatric**: <18years: not established.
- **Geriatrics**: No overall differences observed between younger patients and patients 65 years of age and older.
- **Hepatic impairment**: Avoid use in severe hepatic impairment (Child Pugh C). Consider additional serum K^+ monitoring in patients with moderate hepatic impairment (Child Pugh B).

MPR

Contraindications

- Concomitant treatment with strong CYP3A4 inhibitors (eg, itraconazole).
- Patients with adrenal insufficiency.

Warnings and Precautions

- Increased risk of hyperkalemia in patients with decreasing kidney function and higher baseline potassium levels.
- Measure serum K^+ and eGFR in all patients prior to initiation and adjust dose accordingly.

MPR

Interactions

- Potentiated by strong CYP3A4 inhibitors (eg, itraconazole): see Contraindications.
- Avoid concomitant grapefruit or grapefruit juice.
- Potentiated by moderate or weak CYP3A4 inhibitors (eg, erythromycin, amiodarone); monitor and adjust dose appropriately.
- Antagonized by strong or moderate CYP3A4 inducers (eg, efavirenz, rifampicin); avoid.
- Concomitant use with drugs or supplements that increase serum K^+; monitor serum K^+ more frequently.

MPR

Adverse Reactions

- **Most common (≥ 1% and more frequently than placebo)**: Hyperkalemia, hypotension, hyponatremia.

MPR

Mechanism of Action

- **Finerenone** is a nonsteroidal, selective antagonist of the mineralocorticoid receptor (MR), which blocks MR-mediated sodium reabsorption and MR overactivation in both epithelial (eg, kidney) and nonepithelial (eg, heart, blood vessels) tissues.
- MR overactivation is thought to contribute to fibrosis and inflammation.
- Finerenone has a high potency and selectivity for the MR and has no relevant affinity for androgen, progesterone, estrogen, and glucocorticoid receptors.

Pharmacokinetics

- Steady-state reached after 2 days of dosing.
- **Absorption**: C_{max}: 0.5 to 1.25 hours after dosing.
- **Distribution**: Plasma protein binding: 92% (primarily to serum albumin, in vitro).
- **Metabolism**: CYP3A4 (primary; 90%), and CYP2C8 (minor; 10%).
- **Elimination**: Terminal half-life: 2 to 3 hours.
- **Excretion**: Renal (80%), fecal (20%).

Clinical Trials

- Approval was based on the randomized, double-blind, placebo-controlled, multicenter phase 3 FIDELIO-DKD study that evaluated the efficacy and safety of finerenone, in addition to standard of care, in 5674 patients with chronic kidney disease associated with type 2 diabetes.
- Patients were randomly assigned 1:1 to receive finerenone (n=2833) or placebo (n=2841).
- The **primary composite endpoint** was time to first occurrence of kidney failure, a sustained decrease of at least 40% in eGFR from baseline, or renal death.

MPR

Clinical Trials

- **Patient demographics**
  - Mean age: 66 years.
  - 70% Male; 63% White; 25% Asian; 5% Black.
  - At baseline:
    - Mean eGFR: 44mL/min/1.73m^2, with 55% of patients having an eGFR <45mL/min/1.73m^2.
    - Median urine albumin-to-creatinine ratio: 852mg/g.
    - Mean glycated hemoglobin A1c (HbA1c): 7.7%.
    - 99.8% were treated with an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB).
    - 97% were on an antidiabetic agent; 74% were on a statin; 57% were on an antiplatelet agent.
  - Approximately 46% had a history of atherosclerotic cardiovascular disease.

MPR

Clinical Trials

- After a median follow-up of 2.6 years, results showed that finerenone reduced the incidence of the **primary composite endpoint** of kidney failure, sustained eGFR decline ≥40%, or renal death by 17.8% (n=504/2833) compared with 21.1% (n=600/2841) in patients treated with placebo (hazard ratio [HR], 0.82; 95% CI, 0.73-0.93; *P* =.001).
- Treatment with finerenone was also associated with a lower incidence of the **secondary composite endpoint** of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or hospitalization for heart failure compared with patients treated with placebo (13% [n=367/2833] vs 14.8% [n=420/2841]; HR, 0.86; 95% CI, 0.75-0.99; *P* =.034).

MPR

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/kerendia/