PDL DRUG REVIEW

Proprietary Name: Kerendia®
Common Name: finerenone
PDL Category: Mineralocorticoid Receptor Antagonists

Comparable Products	Preferred Drug List Status
Farxiga	Preferred

Summary

Pharmacology/Usage: Finerenone, the active ingredient of Kerendia®, is a nonsteroidal selective antagonist of the mineralocorticoid receptor (MR), which is activated by aldosterone and cortisol and regulates gene transcription. Finerenone blocks MR mediated sodium reabsorption and MR overactivation in both epithelial (e.g. kidney) and nonepithelial (e.g. heart and 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.

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 adult patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2D).

There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data on the use in pregnancy to assess for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Film-Coated Tablets: 10mg, 20mg

Recommended Dosage: Measure serum potassium levels and estimated glomerular filtration rate (eGFR) before initiation. Do not initiate treatment if serum potassium is >5.0mEq/L.

The recommended starting dose of Kerendia® is based on eGFR and can be seen in the table below, which was adapted from the prescribing information. If not able to swallow whole tablets, Kerendia® may be crushed and mixed with water or soft foods such as applesauce immediately prior to use and administered orally.

eGFR ($ml/min/1.73m^2$)	Starting dose
≥60	20mg QD
≥25 to <60	10mg QD
<25	Not recommended

The target daily dose of Kerendia® is 20mg. Measure serum potassium 4 weeks after starting treatment and adjust dose per the table below, which was adapted from the prescribing information. If serum potassium levels are >4.8 to 5.0 mEq/L, initiation of Kerendia® treatment may be considered with additional serum potassium monitoring within the first 4 weeks based on clinical judgement and serum potassium levels. Monitor serum potassium 4 weeks after a dose adjustment and throughout treatment, and adjust the dose as needed.

	Current Kerendia® dose	
Current serum potassium (mEq/L)	10mg QD	20mg QD
≤4.8	↑ dose to 20mg QD *	Maintain 20mg QD
>4.8 – 5.5	Maintain 10mg QD	Maintain 20mg QD
>5.5	Withhold Kerendia® -Consider restarting at 10mg QD when serum potassium ≤5.0mEq/L	Withhold Kerendia® -Restart at 10mg QD when serum potassium ≤5.0mEq/L

*If eGFR has ↓ by >30% compared to previous measurement, maintain 10mg dose

Dosage adjustment is not recommended in patients with mild or moderate hepatic impairment; however, consider additional serum potassium monitoring in patients with moderate hepatic impairment. Avoid the use of Kerendia® in patients with severe hepatic impairment.

Drug Interactions: Kerendia® is a CYP3A4 substrate. Concomitant use with a strong CYP3A4 inhibitor increases finerenone exposure, which may increase the risk of Kerendia® adverse reactions. Concomitant use of Kerendia® with strong CYP3A4 inhibitors is contraindicated. Avoid concomitant intake of grapefruit or grapefruit juice.

Concomitant use of Kerendia® with a moderate or weak CYP3A4 inhibitor increases finerenone exposure, which may increase the risk of Kerendia® adverse reactions. Monitor serum potassium during drug initiation or dosage adjustment of either Kerendia® or the moderate or weak CYP3A4 inhibitor and adjust Kerendia® dosage as appropriate.

Concomitant use of Kerendia® with a strong or moderate CYP3A4 inducer decreases finerenone exposure, which may reduce the efficacy of Kerendia®. Avoid concomitant use of Kerendia® with strong or moderate CYP3A4 inducers.

More frequent serum potassium monitoring is warranted in patients receiving concomitant therapy of Kerendia® with drugs or supplements that increase serum potassium.

Box Warning: There is no box warning associated with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Kerendia®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than the placebo.* The most frequently reported adverse events included hyperkalemia (9.3%), hypotension (1.4%), and hyponatremia (0.7%). Hospitalization due to hyperkalemia for the Kerendia® group was 1.4% as compared with 0.3% in the placebo group.

Kerendia® can cause hyperkalemia. The risk for developing hyperkalemia increases with decreasing kidney function and is greater in patients with higher baseline potassium levels or other risk factors for hyperkalemia. Measure serum potassium and eGFR in all patients before initiation of treatment with Kerendia® and dose accordingly. Do not start Kerendia® if serum potassium is >5.0mEq/L. In addition, measure serum potassium periodically during treatment with Kerendia® and adjust dose accordingly. More frequent monitoring may be needed for patients at risk for hyperkalemia, including those on concomitant medications that impair potassium excretion or increase serum potassium.

Contraindications: In patients:

- Who are receiving concomitant treatment with strong CYP3A4 inhibitors
- With adrenal insufficiency

Manufacturer: Bayer Healthcare Pharmaceuticals

Analysis: The safety and efficacy of Kerendia® (finerenone) were assessed in a randomized, double-blind, placebo-controlled, multicenter study (FIDELIO-DKD) that included adults with chronic kidney disease (CKD) associated with type 2 diabetes, defined as either having an urinary albumin-to-creatinine ratio (UACR) of 30 to 300mg/g, eGFR 25 to 60ml/min/1.73m^2, and diabetic retinopathy, or as having an UACR of ≥300mg/g and an eGFR of 25 to 75ml/min/1.73m^2. The trial excluded patients with known significant non-diabetic kidney disease.

All included adults were to have a serum potassium ≤4.8mEq/L at screening and be receiving standard of care background therapy, including a maximum tolerated labeled dose of an ACE inhibitor or ARB. Patients with a clinical diagnosis of chronic heart failure with reduced ejection fraction and persistent symptoms were excluded. Patients were randomized to Kerendia® or placebo and were followed for a median of 2.6 years. The mean age of the study population was 66 years, while 70% were male and 63% were white. At baseline, the mean eGFR was 44ml/min/1.73m^2, the median UACR was 852mg/g, and the mean HbA1c was 7.7%. In addition, about 46% of subjects had a history of atherosclerotic cardiovascular disease. Furthermore, at baseline 99.8% of patients were treated with an ACE Inhibitor or ARB, 97% were on an antidiabetic agent, 74% were on a statin, and 57% were on an antiplatelet agent.

The primary objective of the study was to determine whether Kerendia® reduced the incidence of a sustained decline in eGFR of ≥40%, kidney failure (defined as chronic dialysis, kidney transplantation, or a sustained decrease in eGFR to <15ml/min/1.73m^2), or renal death. Results suggested that Kerendia® reduced the incidence of the primary composite endpoint of a sustained decline in eGFR of ≥40%, kidney failure, or renal death (HR 0.82, p=0.001) as compared with placebo. The treatment effect reflected a reduction in a sustained decline in eGFR of ≥40% and progression to kidney failure. There were few renal deaths during the trial.

In addition, Kerendia® also reduced the incidence of the composite endpoint of cardiovascular death, non-fatal MI, non-fatal stroke, or hospitalization for heart failure (HR 0.86, p=0.034). The treatment effect reflected a reduction in CV death, non-fatal MI, and hospitalization for heart failure. Results of both endpoints can be seen in the table below, which was adapted from the prescribing information.

Primary & Secondary Time-to-event Endpoints	Kerendia® (N=2833)		Placebo (N=2841)		Treatment effect
	n (%)	Event rate (100 pt-year)	n (%)	Event rate (100 pt-year)	HR; p-value
Primary composite	504 (17.8%)	7.6	600 (21.1%)	9.1	0.82; p=0.001 (NNT=31)
Kidney failure	208 (7.3%)	3.0	235 (8.3%)	3.4	0.87
Sustained eGFR decline ≥40%	479 (16.9%)	7.2	577 (20.3%)	8.7	0.81
Renal death	2 (<0.1%)	-	2 (<0.1%)	-	-
Secondary composite	367 (13%)	5.1	420 (14.8%)	5.9	0.86; p=0.034 (NNT=56)
CV death	128 (4.5%)	1.7	150 (5.3%)	2.0	0.86
Non-fatal MI	70 (2.5%)	0.9	87 (3.1%)	1.2	0.8

Primary & Secondary Time-to-event Endpoints	Kerendia® (N=2833)		Placebo (N=2841)		Treatment effect
	n (%)	Event rate (100 pt-year)	n (%)	Event rate (100 pt-year)	HR; p-value
Non-fatal stroke	90 (3.2%)	1.2	87 (3.1%)	1.2	1.03
Hospitalization for heart failure	139 (4.9%)	1.9	162 (5.7%)	2.2	0.86

Note: Time to first event was analyzed in a Cox proportional hazards model. For patients with multiple events, only the first event contributed to the composite endpoint. Sums of the numbers of first events for the single components do not add up to the numbers of events in the composite endpoint. (pt-year: patient year)

Place in Therapy: Kerendia® is an oral nonsteroidal selective antagonist of the mineralocorticoid receptor that is indicated to reduce the risk of sustained eGFR decline, end-stage kidney disease, cardiovascular death, non-fatal MI, and hospitalization for heart failure in adults with chronic kidney disease (CKD) associated with type 2 diabetes (T2D). In a phase 3 study, Kerendia® significantly reduced the incidence of the primary composite endpoint of a sustained decline in eGFR of ≥40%, kidney failure, or renal death (HR 0.82, p=0.001; NNT = 31) when added to standard of care background therapy as compared with placebo added to standard of care background therapy. The treatment effect reflected a reduction in a sustained decline in eGFR of ≥40% and progression to kidney failure. In addition, Kerendia® also significantly reduced the incidence of the composite endpoint of CV death, non-fatal MI, non-fatal stroke, or hospitalization for heart failure (HR 0.86, p=0.034; NNT =56) as a secondary endpoint as compared to placebo. The treatment effect reflected a reduction in CV death, non-fatal MI, and hospitalization for heart failure.

There is some evidence at this time to suggest that Kerendia® added to standard of care background therapy is more effective than placebo added to standard of care background therapy for the primary and secondary composite endpoints of a phase 3 study; however, there is no evidence at this time to support that Kerendia® is safer or more effective than the other currently preferred, more cost-effective medications. It is therefore recommended that Kerendia® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred**

References

[1] Kerendia [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals; 2021.