NEW DRUG APPROVAL

Brand Name	Kerendia®
Generic Name	finerenone
Drug Manufacturer	Bayer HealthCare Pharmaceuticals Inc

New Drug Approval

FDA Approval Date: July 09, 2021
Review Designation: Priority
Type of Review: Type 1 - New Molecular Entity; New Drug Application (NDA): 215341
Dispensing Restrictions: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Chronic kidney disease (CKD) is common in people with both type 1 and type 2 diabetes. It is defined by the presence of reduced glomerular filtration rate (GFR) and/or increased urinary albumin excretion for at least three months.

Globally, DKD is a major cause of CKD and is the most common cause of end-stage kidney disease (ESKD). As an example, in the United States in 2017, diabetes was reported as a primary etiology in nearly one-half of all patients diagnosed with ESKD. The prevalence of diabetes in the United States has increased over the last 20 years from 6 to 10 percent, the proportion of people with diabetes who also have CKD has remained relatively stable (approximately 25 to 30 percent). However, the distribution of clinical manifestations of diabetic kidney disease has changed.

Despite the high prevalence of kidney disease among people with diabetes, CKD awareness is extremely poor, even in the United States. Only 10 percent of people with stage 3 CKD (eGFR 30 to 59 mL/min/1.73 m2) are aware of their diagnosis; although this proportion is higher among people with stage 4 CKD (eGFR 15 to 29 mL/min/1.73 m2), less than 60 percent of patients overall are aware of their disease.

Efficacy

The FIDELIO-DKD study was a randomized, double-blind, placebo-controlled, multicenter study in adult patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2D).

Table - Analysis of the Primary and Secondary Time-to-Event Endpoints (and their Individual Components) in Phase 3 Study FIDELIO-DKD

	Kerendia N=2833		Placebo N=2841		Treatment Effect Kerendia / Placebo	
Primary and Secondary Time-to-event Endpoints:	**n (%)**	**Event Rate (100 pt-yr)**	**n (%)**	**Event Rate (100 pt-yr)**	**Hazard Ratio (95% CI)**	**p-value**
Primary composite of kidney failure, sustained eGFR decline ≥40% or renal death	504 (17.8%)	7.6	600 (21.1%)	9.1	0.82 [0.73; 0.93]	0.001
Kidney failure	208 (7.3%)	3.0	235 (8.3%)	3.4	0.87 [0.72; 1.05]	-
Sustained eGFR decline ≥40%	479 (16.9%)	7.2	577 (20.3%)	8.7	0.81 [0.72; 0.92]	-
Renal death	2 (<0.1%)	-	2 (<0.1%)	-	-	-
Secondary composite of CV death, non-fatal MI, non-fatal stroke or hospitalization for heart failure	367 (13.0%)	5.1	420 (14.8%)	5.9	0.86 [0.75; 0.99]	0.034
CV death	128 (4.5%)	1.7	150 (5.3%)	2.0	0.86 [0.68;1.08]	-
Non-fatal MI	70 (2.5%)	0.9	87 (3.1%)	1.2	0.80 [0.58;1.09]	-
Non-fatal stroke	90 (3.2%)	1.2	87 (3.1%)	1.2	1.03 [0.76;1.38]	-
Hospitalization for heart failure	139 (4.9%)	1.9	162 (5.7%)	2.2	0.86 [0.68;1.08]	-

p-value: two-sided p-value from stratified logrank test

CI = confidence interval, CV = cardiovascular, eGFR = estimated glomerular filtration rate, MI = myocardial infarction, N = number of subjects, n = number of subjects with event, pt-yr = patient year.
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.

Safety

ADVERSE EVENTS

Adverse reactions occurring in ≥ 1% of patients on Kerendia® and more frequently than placebo is hyperkalemia, hypotension, and hyponatremia.

WARNINGS & PRECAUTIONS

Hyperkalemia: Patients with decreased kidney function and higher baseline potassium levels are at increased risk. Monitor serum potassium levels and adjust dose as needed.

CONTRAINDICATIONS

- Concomitant use with strong CYP3A4 inhibitors.
- Patients with adrenal insufficiency.

Clinical Pharmacology

MECHANISMS OF ACTION

Finerenone 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.

Dose & Administration

ADULTS

20 mg orally once daily. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary.

PEDIATRICS

Safety and efficacy have not been established.

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

- eGFR 60 mL/minute/1.73 m^2 or more: No dosage adjustment necessary.
- eGFR 25 to 59 mL/minute/1.73 m^2: 10 mg orally once daily initially; may increase to 20 mg orally once daily after 4 weeks if serum potassium concentration is 4.8 mEq/L or less and eGFR has not decreased by more than 30% compared to previous measurement.
- eGFR less than 25 mL/minute/1.73 m^2: Use not recommended.

HEPATIC IMPAIRMENT

- Mild or moderate hepatic impairment (Child Pugh A or B): No dosage adjustment necessary.
- Severe hepatic impairment (Child Pugh C): Avoid use.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Tablets: 10 mg and 20 mg