



מרץ 2023

רופא/ה נכבד/ה,
רוקח/ת נכבד/ה,

הנדון:
Kerendia 10 mg
Kerendia 20 mg
Film coated tablets
Finerenon 10mg, 20mg

אנו מבקשים להודיעכם שהעלון לצרכן של התכשיר עודכן.

ההתוויה המאושרת לתכשיר:

Kerendia is indicated 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).

בהודעה זו כלולים העידכונים המהותיים בלבד. בפירוט שלהלן מופיע, מתוך כל פרק ששונה בעלוני, רק המידע שהתעדכן. תוספת טקסט מסומנת בקו תחתון, מחיקת טקסט מסומנת בקו חוצה.

העדכונים בעלון לרופא

8.1 Clinical Trials Experience

The most frequently reported ($\geq 10\%$) adverse reaction in both studies was hyperkalemia [see *Warnings and Precautions (7.1)*]. Hospitalization due to hyperkalemia for the Kerendia group was 0.9% versus 0.2% in the placebo group across both studies. Hyperkalemia led to permanent discontinuation of treatment in 1.7% receiving Kerendia versus 0.6% of patients receiving placebo across both studies.

10 USE IN SPECIFIC POPULATIONS

10.5 Geriatric Use

Of the ~~6510~~ 2827 patients who received Kerendia in the FIDELIO-DKD and FIGARO-DKD studies ~~FIDELIO-DKD study~~, 55 58% of patients were 65 years and older, and 14% ~~45%~~ were 75 years and older. No overall differences in safety or efficacy were observed between these patients and younger patients. No dose adjustment is required.

13 CLINICAL PHARMACOLOGY

13.2 Pharmacodynamics

In FIDELIO-DKD and FIGARO-DKD, randomized, double-blind, placebo-controlled, multicenter studies in adult patients with chronic kidney disease associated with type 2 diabetes, the placebo-corrected relative reduction in urinary albumin-to-creatinine ratio (UACR) in patients randomized to finerenone was 31% (95% CI 29-34%) and 32% (95% CI 30-35%) respectively at Month 4 and remained stable for the duration of the trial.



In ARTS DN, a randomized, double-blind, placebo-controlled, multicenter phase IIb dose finding study in adults with CKD and T2D, the placebo-corrected relative reduction in UACR at Day 90 was 25% and 38% in patients treated with finerenone 10 mg and 20 mg once daily, respectively.

13.3 Pharmacokinetics

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Multiple doses of 40 mg finerenone once-daily had no clinically relevant effect on AUC or C_{max} of the BCRP and OATP substrate rosuvastatin.

15 CLINICAL STUDIES

...

FIGARO-DKD

The FIGARO-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), defined as either having a UACR of ≥ 30 mg/g to <300 mg/g and an eGFR of 25 to 90 mL/min/1.73m², or a UACR > 300 mg/g and an eGFR > 60 mL/min/1.73m² at screening. Patients were required to have a serum potassium of ≤ 4.8 mmol/L at screening and received standard of care background therapy, including a maximum tolerated labeled dose of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB).

The primary endpoint of the FIGARO-DKD study was a composite of time to first occurrence of CV death, non-fatal MI, non-fatal stroke or hospitalization for heart failure. The secondary endpoint included a composite of time to kidney failure, a sustained decline in eGFR of 40% or more compared to baseline over at least 4 weeks, or renal death.

A total of 7,352 patients were randomized to receive Kerendia (N=3686) or placebo (N=3666) and were followed for a median of 3.4 years. The mean age of the study population was 64 years, and 69% of patients were male. The global trial population was 72% White, 20% Asian and 4% Black (18.5% Black in the US). At baseline, the mean eGFR was 67.8 mL/min/1.73 m², with 62% of patients having an eGFR ≥ 60 mL/min/1.73 m². Median urine to albumin-to-creatinine ratio (UACR) was 308 mg/g, and mean glycated hemoglobin A1c (HbA1c) was 7.7%. Approximately 45% of patients had a history of atherosclerotic cardiovascular disease, 8% had a history of cardiac failure, and the mean blood pressure was 136/77 mmHg.

At baseline, 99.9% of patients were treated with an ACEi or ARB. Approximately 98% were on an antidiabetic agent (insulin [54%], biguanides [69%], glucagon-like peptide-1 [GLP-1] receptor agonists [7%], sodium-glucose cotransporter 2 [SGLT2] inhibitors [8%]). The other most frequent medication class taken at baseline was statins (71 %).

Kerendia reduced the incidence of the primary composite endpoint of CV death, non-fatal MI, non-fatal stroke or hospitalization for heart failure compared to placebo in a time to event analysis using the Cox proportional hazards model and log rank test (HR 0.87, 95% CI 0.76-0.98, p = 0.0264). See Figure 3/Table 4 below. The treatment effect reflected a reduction in hospitalization for heart failure and CV death. The treatment effect on the primary composite endpoint was generally consistent across subgroups, including patients with and without pre-existing cardiovascular disease.

Kerendia numerically reduced the incidence of the composite endpoint of kidney failure, sustained eGFR decline of 40% or more or renal death was observed in the Kerendia group compared to placebo (HR 0.87, 95% CI 0.76-1.01, p=0.0689). The treatment effect reflected a reduction in a sustained



decline in eGFR of $\geq 40\%$ and progression to kidney failure. There were few renal deaths during the trial. See Figure 4/Table 5 below.

Table 5: Analysis of the Primary and Secondary Time-to-Event Endpoints (and their Individual Components) in Phase III Study FIGARO-DKD

Primary and Secondary Time-to-event Endpoints:	Kerendia* N=3686		Placebo* N=3666		Treatment Effect Kerendia / Placebo	
	n (%)	Event Rate (100 pt-yr)	n (%)	Event Rate (100 pt-yr)	Hazard Ratio (95% CI)	p-value
Primary composite of CV death, non-fatal MI, non-fatal stroke or hospitalization for heart failure	458 (12.4%)	3.9	519 (14.2%)	4.5	0.82 [0.76; 0.98]	0.0264
CV death	194 (5.3%)	1.6	214 (5.8%)	1.8	0.90 [0.74; 1.09]	-
Non-fatal MI	103 (2.8%)	0.9	102 (2.8%)	0.9	0.99 [0.76; 1.31]	-
Non-fatal stroke	108 (2.9%)	0.9	111 (3.0%)	0.9	0.97 [0.74; 1.26]	-
Hospitalization for heart failure	117 (3.2%)	1.0	163 (4.4%)	1.4	0.71 [0.56; 0.90]	-
Composite of kidney failure, sustained eGFR decline $\geq 40\%$ or renal death	350 (9.5%)	3.2	395 (10.8%)	3.6	0.87 [0.76; 1.01]	0.0689
Kidney Failure	46 (1.2%)	0.4	62 (1.7%)	0.5	0.72 [0.49; 1.05]	-
Sustained eGFR decline $\geq 40\%$	338 (9.2%)	3.0	385 (10.5%)	3.5	0.87 [0.75; >1.00]	-
Renal death	0	-	2 (< 0.1%)	-	-	-

* Treatment in addition to maximum tolerated labeled doses of ACEi or ARB

16.1 How Supplied

... blister stripe of 14, 28 or 98 film-coated tablets or perforated unit dose blisters in cartons of 10×1 or 100×1 film-coated tablets

Not all pack sizes are marketed.

העלון לצרכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:
<https://data.health.gov.il/drugs/index.html#!/byDrug>

ניתן לקבלו מודפס ע"י פניה לחברת באייר ישראל, רח' החרש 36 הוד השרון, טלפון: 09-7626700.

בברכה,
 באייר ישראל