

The Medical Letter[®]

on Drugs and Therapeutics

Volume 65

January 23, 2023

ISSUE No.
1668

IN THIS ISSUE

In Brief: Finerenone (*Kerendia*) for Diabetic Kidney Disease.....p 15

Important Copyright Message

FORWARDING OR COPYING IS A VIOLATION OF U.S. AND INTERNATIONAL COPYRIGHT LAWS

The Medical Letter, Inc. publications are protected by U.S. and international copyright laws. Forwarding, copying, or any distribution of this material without permission to a nonsubscriber is prohibited.

Sharing a password with a nonsubscriber or otherwise making the contents of this site available to third parties is prohibited.

By accessing and reading the attached content I agree to comply with U.S. and international copyright laws and these terms and conditions of The Medical Letter, Inc.

**For further information click: [Subscriptions](#), [Site Licenses](#), [Reprints](#)
or call customer service at: 800-211-2769**

The Medical Letter[®]

on Drugs and Therapeutics

Volume 65 (Issue 1668)

January 23, 2023

Take CME Exams

IN BRIEF

Finerenone (*Kerendia*) for Diabetic Kidney Disease

Recently published guidelines from the American Diabetes Association (ADA) and the Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group recommend addition of the oral nonsteroidal mineralocorticoid receptor antagonist (MRA) finerenone (*Kerendia*) to standard treatment in patients with type 2 diabetes and chronic kidney disease (CKD).^{1,2}

FINERENONE – Finerenone was approved by the FDA in 2021 to reduce the risk of sustained eGFR decline, end-stage kidney disease, nonfatal myocardial infarction (MI), hospitalization for

heart failure (HF), and cardiovascular death in adults with CKD associated with type 2 diabetes.³ It inhibits aldosterone at the mineralocorticoid receptor, preventing receptor overactivation and decreasing the inflammation and fibrosis that lead to kidney dysfunction and cardiovascular disease. Like the steroidal MRAs spironolactone (*Aldactone*, and others) and eplerenone (*Inspira*, and generics), finerenone reduces albuminuria, but it appears to cause less hyperkalemia.

STANDARD TREATMENT – Patients with CKD associated with type 2 diabetes are usually treated with an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB), in addition to a statin and metformin. A sodium-glucose cotransporter 2 (SGLT2) inhibitor is often added to slow progression of CKD and reduce the risk of cardiovascular events (see Table 1).^{1,2}

CLINICAL STUDIES – The recent recommendations were based on the results of two double-blind trials (FIDELIO-DKD and FIGARO-DKD) in patients with CKD and type 2 diabetes with or without cardiovascular disease. In both trials, patients were randomized to receive finerenone or placebo once

Table 1. Treatment of CKD¹ Associated with Type 2 Diabetes²

- ▶ A maximally tolerated dose of a renin-angiotensin system (RAS) inhibitor (ACE inhibitor or ARB) is recommended for patients with hypertension and albuminuria³
- ▶ A statin⁴ is recommended for all patients
- ▶ Metformin is recommended for patients with an eGFR ≥ 30 mL/min/1.73 m²
- ▶ An SGLT2 inhibitor with proven renal benefits (canagliflozin, dapagliflozin, or empagliflozin) should be added in patients with an eGFR ≥ 20 mL/min/1.73 m² and albuminuria⁵
- ▶ Addition of finerenone is recommended for patients with an eGFR ≥ 25 mL/min/1.73 m², normal serum potassium levels, and an albumin-to-creatinine ratio ≥ 30 mg/g despite a maximally tolerated dose of a RAS inhibitor

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GLP-1 = glucagon-like peptide 1; SGLT2 = sodium-glucose cotransporter 2

1. CKD is defined as: persistent eGFR < 60 mL/min/1.73 m², albuminuria (ACR ≥ 30 mg/g), or other markers of kidney damage, such as hematuria or structure abnormalities; persistence for ≥ 3 months is required for diagnosis. Kidney Disease Improving Global Outcomes (KDIGO) Diabetes Working Group. *Kidney Int* 2022; 102(5S):S1.
2. Adapted from IH de Boer et al. Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). *Diabetes Care* 2022; 45:3075.
3. Dihydropyridine calcium channel blockers and thiazide-like diuretics can be used in patients with hypertension who do not have albuminuria for whom cardiovascular events and mortality are more common than kidney failure.
4. Moderate intensity for primary prevention of atherosclerotic cardiovascular disease (ASCVD) or high intensity for patients with known ASCVD and some patients with multiple ASCVD risk factors.
5. A GLP-1 receptor agonist with proven cardiovascular benefits (dulaglutide, liraglutide, or subcutaneous semaglutide) can be used if an SGLT2 inhibitor is not tolerated and/or additional glycemic lowering is needed. Addition of an SGLT2 inhibitor or a GLP-1 receptor agonist is recommended for patients with CKD without albuminuria.

Table 2. Finerenone Clinical Trial Results

Regimen	Sustained decline in eGFR $\geq 40\%$, renal failure, or renal death	CV death, nonfatal MI, nonfatal stroke, or hospitalization for HF
FIDELIO-DKD (n=5734)¹		
Finerenone ²	17.8%*	13.0%*
Placebo ²	21.1%	14.8%
NNT	30.0	54.7
FIGARO-DKD (n=7437)³		
Finerenone ²	9.5%*	12.4%*
Placebo ²	10.8%	14.2%
NNT	78.2	57.7

*Statistically significant difference vs placebo; CV = cardiovascular; eGFR = estimated glomerular filtration rate; HF = heart failure; MI = myocardial infarction; NNT = number needed to treat to prevent one episode of the composite endpoint

1. Patients had a urine albumin-to-creatinine ratio of 30- <300 mg/g, an eGFR of 25- <60 mL/min/1.73 m², and diabetic retinopathy or a urine albumin-to-creatinine ratio of 300-5000 mg/g and an eGFR 25- <75 mL/min/1.73 m². G Bakris et al. *N Engl J Med* 2020; 383:2219.
2. In addition to an ACE inhibitor or an ARB.
3. Patients had a urine albumin-to-creatinine ratio of 30- <300 mg/g and an eGFR of 25-90 mL/min/1.73 m² or a urine albumin-to-creatinine ratio of 300-5000 mg/g and an eGFR ≥ 60 mL/min/1.73 m². B Pitt et al. *N Engl J Med* 2021; 385:2252.

daily in addition to a maximally tolerated dose of an ACE inhibitor or ARB. Most of the patients in FIDELIO-DKD had severely elevated albuminuria; in FIGARO-DKD, they had less severe albuminuria. In both studies, few patients were taking an SGLT2 inhibitor. Over median follow-up periods of 2.6 years (FIDELIO-DKD) and 3.4 years (FIGARO-DKD), the incidence of a composite of sustained decline in eGFR $\geq 40\%$, renal failure, or renal death and the incidence of a composite of cardiovascular death, nonfatal MI, nonfatal stroke, or hospitalization for HF were statistically significantly lower with finerenone than with placebo (see Table 2).⁴⁻⁶

ADVERSE EFFECTS – Hyperkalemia was the most common adverse effect of finerenone in FIDELIO-DKD and FIGARO-DKD. Hypotension and hyponatremia also occurred.

DOSAGE, ADMINISTRATION, AND COST – The recommended starting dosage of finerenone is 10 mg (eGFR ≥ 25 - <60 mL/min/1.73 m²) or 20 mg (eGFR ≥ 60 mL/min/1.73 m²) once daily; after 4 weeks, the 10-mg dose can be increased to 20 mg. Finerenone should not be started in patients with a serum potassium level >5.0 mEq/L. Serum potassium levels should be monitored during treatment; the drug should be withheld when levels are >5.5 mEq/L. Finerenone is not recommended for use in patients with an eGFR <25 mL/min/1.73 m² or in those with severe hepatic impairment (Child-Pugh C). A 30-day supply of *Kerendia* costs \$597.60.⁷

CONCLUSION – Addition of the oral nonsteroidal mineralocorticoid receptor antagonist (MRA)

finerenone (*Kerendia*) to standard treatment is now recommended to slow progression of kidney disease and reduce the risk of cardiovascular events in patients with type 2 diabetes and chronic kidney disease (CKD). Finerenone has been shown to modestly improve renal and cardiovascular outcomes compared to placebo in patients with type 2 diabetes and CKD, most of whom were not taking an SGLT2 inhibitor concomitantly. Finerenone is expensive and causes hyperkalemia. How steroidal MRAs such as spironolactone and eplerenone compare to finerenone in improving renal and cardiovascular outcomes in patients with type 2 diabetes and CKD remains to be determined. ■

1. American Diabetes Association Professional Practice Committee. 11. Chronic kidney disease and risk management: standards of medical care in diabetes—2022. *Diabetes Care* 2022; 45(Suppl 1):S175.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 clinical practice guidelines for diabetes management in chronic kidney disease. *Kidney Int* 2022; 102(5S):S1.
3. Finerenone (Kerendia) for chronic kidney disease. *Med Lett Drugs Ther* 2021; 63:131.
4. GL Bakris et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. *N Engl J Med* 2020; 383:2219.
5. G Filippatos et al. Finerenone and cardiovascular outcomes in patients with chronic kidney disease and type 2 diabetes. *Circulation* 2021; 143:540.
6. B Pitt et al. Cardiovascular events with finerenone in kidney disease and type 2 diabetes. *N Engl J Med* 2021; 385:2252.
7. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. January 5, 2023. Reprinted with permission by First Databank, Inc. All rights reserved. ©2023. www.fdbhealth.com/policies/drug-pricing-policy.

PRESIDENT: Mark Abramowicz, M.D.; **VICE PRESIDENT, EDITOR IN CHIEF:** Jean-Marie Pflomm, Pharm.D.; **ASSOCIATE EDITORS:** Susan M. Daron, Pharm.D., Amy Faucard, MLS, Michael P. Viscusi, Pharm.D. **CONSULTING EDITORS:** Joanna Esterow, PA-C, Mordechai Sacks, DMSc, PA-C, Brinda M. Shah, Pharm.D., F. Peter Swanson, M.D.

CONTRIBUTING EDITORS: Carl W. Bazil, M.D., Ph.D., Columbia University College of Physicians and Surgeons; Ericka L. Crouse, Pharm.D., B.C.P.P., C.G.P., F.A.S.H.P., F.A.S.C.P., Virginia Commonwealth University; Vanessa K. Dalton, M.D., M.P.H., University of Michigan Medical School; Eric J. Epstein, M.D., Albert Einstein College of Medicine; David N. Juurlink, BPhm, M.D., Ph.D., Sunnybrook Health Sciences Centre; Richard B. Kim, M.D., University of Western Ontario; Sandip K. Mukherjee, M.D., F.A.C.C., Yale School of Medicine; Dan M. Roden, M.D., Vanderbilt University School of Medicine; Esperance A.K. Schaefer, M.D., M.P.H., Harvard Medical School; Neal H. Steigbigel, M.D., New York University School of Medicine; Arthur M. F. Yee, M.D., Ph.D., F.A.C.R., Weill Medical College of Cornell University

MANAGING EDITOR AND DIRECTOR OF CONTENT OPERATIONS: Susie Wong; **EDITORIAL ASSISTANT:** Karrie Ferrara

FULFILLMENT AND SYSTEMS MANAGER: Cristine Romatowski; **EXECUTIVE DIRECTOR OF SALES:** Elaine Reaney-Tomaselli
EXECUTIVE DIRECTOR OF MARKETING AND COMMUNICATIONS: Joanne F. Valentino; **INTERIM PUBLISHER:** Jean-Marie Pflomm, Pharm.D.

Founded in 1959 by Arthur Kallet and Harold Aaron, M.D.

Copyright and Disclaimer: The Medical Letter, Inc. is an independent nonprofit organization that provides healthcare professionals with unbiased drug prescribing recommendations. The editorial process used for its publications relies on a review of published and unpublished literature, with an emphasis on controlled clinical trials, and on the opinions of its consultants. The Medical Letter, Inc. does not sell advertising or receive any commercial support. No part of the material may be reproduced or transmitted by any process in whole or in part without prior permission in writing. The Medical Letter, Inc. does not warrant that all the material in this publication is accurate and complete in every respect. The Medical Letter, Inc. and its editors shall not be held responsible for any damage resulting from any error, inaccuracy, or omission.

Subscription Services

Address:

The Medical Letter, Inc.
145 Huguenot St. Ste. 312
New Rochelle, NY 10801-7537
www.medicalletter.org

Customer Service:

Call: 800-211-2769 or 914-235-0500
Fax: 914-632-1733
E-mail: custserv@medicalletter.org

Permissions:

To reproduce any portion of this issue,
please e-mail your request to:
permissions@medicalletter.org

Subscriptions (US):

1 year - \$159; 2 years - \$298;
3 years - \$398. \$65 per year
for students, interns, residents,
and fellows in the US and Canada.
Reprints - \$45 per issue or article

Site License Inquiries:

E-mail: SubQuote@medicalletter.org
Call: 800-211-2769
Special rates available for bulk
subscriptions.