FINERON

Finerenone Tablets 10/20 mg

PRODUCT MONOGRAPH

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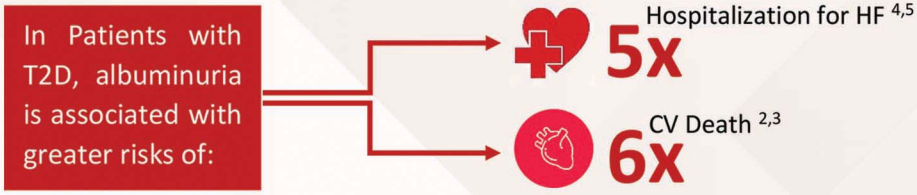
INTRODUCTION

Patients with chronic kidney disease (CKD) and type 2 diabetes face increased risks of kidney progression and cardiovascular complications. Despite current standards of care, many remain vulnerable.

The tipping point of UACR > 30 mg/g indicates the residual risk of CV death and CKD progression. Even a single point of chaos in chronic disease can disrupt the entire interconnected system of the body, especially for the patients with T2D and CKD.

Finerenone: a novel non-steroidal mineralocorticoid receptor antagonist (ns-MRA), offers a new evidence-based option to address these challenges.



PRODUCT INFORMATION

Description

Finerenone is a 3rd generation, Non-Steroidal, Highly Selective Mineralocorticoid Receptor Antagonist (MRAs) which overcomes many limitations of older steroidal MRAs. The distinct features of Finerenone is:

- No hormonal side effects like gynecomastia and menstrual disturbances.
- A short plasma half-life with no active metabolites, and the equal distribution to heart and kidneys are considered to enable finerenone to have minimal effects on serum (K+)

Finerenone reduces the risk of kidney function decline, **kidney failure**, cardiovascular death and hospitalization for **heart failure** in adults with chronic kidney disease associated with **type 2 diabetes**.

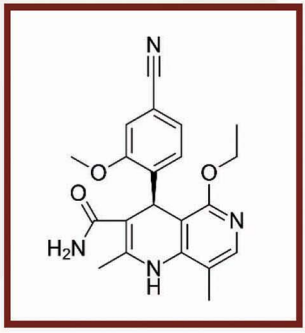


Figure 1. Structure of Finerenone, (C21H22N4O3)

CLINICAL PHARMACOLOGY

Mechanism of Action

Mineralocorticoid receptor overactivation may lead to inflammation and scarring in the kidneys, heart and blood vessels

Finerenone is a nonsteroidal selective antagonist of the mineralocorticoid receptor (MR) which is activated by aldosterone and cortisol and regulates gene transcription. Its binding to the MR leads to a specific receptor-ligand complex that blocks recruitment of transcriptional coactivators implicated in the expression of pro-inflammatory and pro-fibrotic mediators.

Figure 2 Mechanism of Action of Finerenone

Pharmacokinetics and pharmacodynamic

Pharmacokinetics of finerenone are linear and its half-life is 2 to 3 hours, in the dose range of up to 20 mg. Cytochrome P450 (CYP)3A4 (90%) and CYP2C8 (80%) are involved in the extensive biotransformation of finerenone to pharmacologically inactive metabolites, which are excreted via both renal (80%) and biliary (20%) routes. Finerenone is approximated ~ 100% absorption with absolute bioavailability of 43.5% [6].

Structural Properties	Flat (Steroidal)	Flat (Steroidal)	Bulky (Non-steroidal)
Potency to MR	+++	+	+++
Selectivity to MR	+	++	+++
Hormonal Side Effect	++	+	-
Half-Life	> 20 hour	4-6 hour	2-3 hour
Active Metabolites	++	-	-
Tissue distribution	6 fold more in kidney	3 fold more in kidney	Equal distribution

Figure 3 Superior Action of Finerenone Over Steroidal MRAs

INDICATIONS AND USAGE

Finerenone is indicated for the treatment of chronic kidney disease (CKD) with albuminuria associated with type 2 diabetes in adults.
Finerenone has beneficial effect on heart failure with mildly reduced (HFmrEF) or preserved ejection fraction (HFpEF)[7].

DOSAGE AND ADMINISTRATION

Initiation of treatment

Estimated Glomerular Filtration Rate (eGFR) and serum potassium have to be measured to determine initiation the starting dose.

eGFR: ≥ 60	Initiate 20 mg starting dose
eGFR: ≥ 25 and < 60	Initiate 10 mg starting dose
eGFR: < 25	Initiation not recommended

Continuation of treatment and dose adjustment

Serum Potassium (mmol/L)	Finerenone Dose (Once Daily)
≤ 4.8	Increase to or maintain **20 mg once daily**
> 4.8 to 5.0	**Maintain current dose** Either 10 or 20 mg once daily
> 5.0	**Withhold treatment** Restart at 10 mg once daily when [K+] is ≤ 5.0 mmol/L

Monitoring of Serum Potassium to adjust Finerenone dose

Serum potassium must be remeasured **4 weeks** after:

- Initiation of treatment
- Restarting treatment
- Dost adjustment

Method of administration

Oral Use: Tablets may be taken with a glass of water with or without food. Tablets should not be taken with grapefruit or grape fruit juice.

Crushing of tablets: For patients who are unable to swallow whole tablets, finerenone may be crushed and mixed with water or soft foods, such as apple sauce, directly before oral use.

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients. Concomitant treatment with strong inhibitors of CYP3A4, e.g.,

- Itraconazole
- Ketoconazole
- Ritonavir
- Nelfinavir
- Cobicistat
- Clarithromycin
- Telithromycin
- Nefazodone
- Addison's disease

WARNING AND SPECIAL PRECAUTION

Hyperkalemia

Hyperkalemia has been observed in patients treated with finerenone. Some patients are at a higher risk to develop hyperkalemia. Risk factors include low eGFR, higher serum potassium and previous episodes of hyperkalemia. In these patients more frequent monitoring has to be considered. Finerenone should not be given concomitantly with:

- Potassium-sparing diuretics (e.g., amiloride, triamterene) and
- Other mineralocorticoid receptor antagonists (MRAs), e.g., eplerenone, esaxerenone, spironolactone.

Renal Impairment

The risk of hyperkalemia increases with decreasing renal function. Monitoring of renal function should be performed. Finerenone treatment should not be initiated in patients with eGFR < 25 mL/min/1.73 m^2.

Hepatic impairment

Finerenone treatment should not be initiated in patients with severe hepatic impairment. No initial dose adjustment is required in mild hepatic impairment and potassium monitoring is necessary in moderate hepatic impairment according to patient's characteristics.

Heart Failure

Although Finerenone has beneficial role in heart failure with mildly reduced (HFmrEF) and preserved ejection fraction (HFpEF), it should not be initiated in patients with heart failure with reduced ejection fraction (HFrEF) and New York Heat Association (NYHA) II-IV.

Concomitant use of substances that affect finerenone exposure.

Serum potassium should be monitored during concomitant use with moderate or weak CYP3A4 inhibitors. Finerenone should not be used concomitantly with strong or moderate CYP3A4 inducers. Grapefruit or grapefruit juice should not be consumed during finerenone treatment.

Embryo-foetal toxicity

Finerenone should not be used during pregnancy. Women of childbearing with finerenone treatment should be advised to use effective contraception. Women should be advised not to breast-feed during finerenone treatment.

Pediatric population

The safety and efficacy of finerenone in children under 18 years have not yet been established. No data are available.

DRUG AND FOOD INTERACTIONS OF FINERENONE

Concomitant use contraindicated

Strong CYP3A4 inhibitors, since a marked increase in finerenone exposure is expected.

Concomitant use not recommended

Strong and moderate CYP3A4 inducers (like carbamazepine, phenytoin, efavirenz) which are expected to markedly decrease finerenone plasma concentration and result in reduced therapeutic effects. Certain medications that increase serum potassium level due to the risk of hyperkalemia. Grapefruit or grapefruit juice should not be consumed during finerenone treatment.

ADVERSE REACTION OF FINERENONE

Very Common:

- Hyperkalemia (14%)

Common

- Hyponatremia
- Hyperuricemia
- Hypotension
- Pruritus
- Glomerular Filtration Rate Decrease

Uncommon

- Hemoglobin decrease

CLINICAL TRIALS

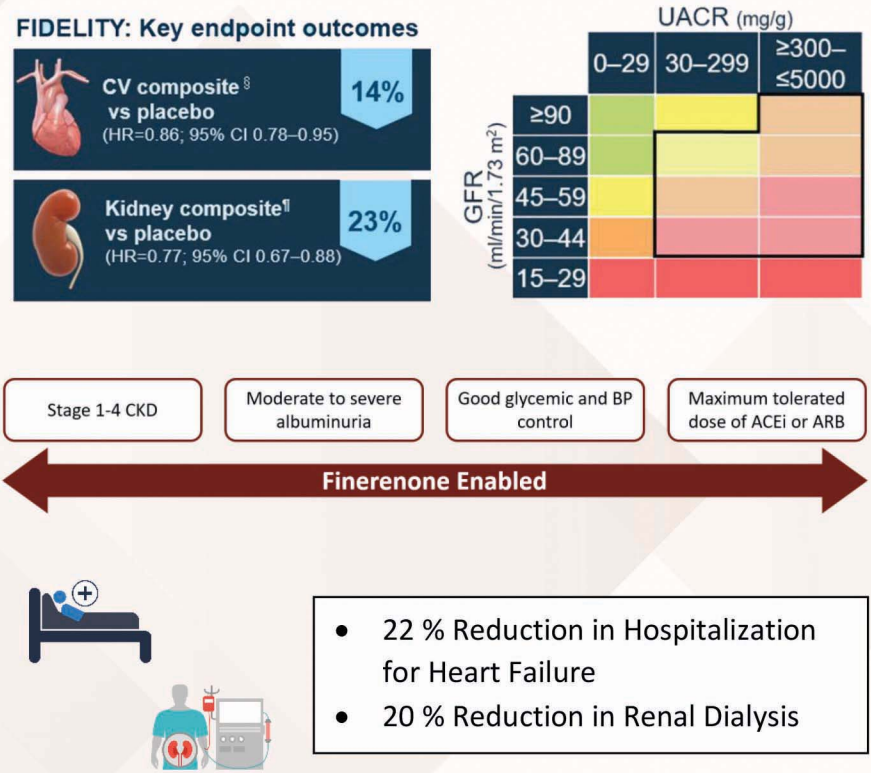
FIDELIO-DKD & FIGARO-DKD Trials [8,9]

	FIDELIO-DKD Main Stage 3-4 CKD n = 5,734	FIGARO-DKD Main Stage 1-2 CKD n = 7,437
Primary Outcome	Reduce 18% CKD progression	Reduce 13% CVD Mortality & Morbidity
Secondary Outcome	Reduce 14% CVD Mortality & Morbidity	Reduce 13% CKD progression
Safety	Small and manageable hyperkalemia risk with minimal clinical effect.	

FIDELIO-DKD: Conclusion - Patients with CKD and type 2 diabetes, treatment with finerenone resulted in lower risks of CKD progression and cardiovascular events than placebo[8].

FIGARO-DKD: Conclusion - Patients with type 2 diabetes and stage 2 to 4 CKD with moderately elevated albuminuria or stage 1 or 2 CKD with severely elevated albuminuria, finerenone therapy improved cardiovascular outcomes as compared with placebo[9].

FIDELITY Prespecified Pooled Analysis of FIDELIO-DKD and FIGARO-DKD [10]

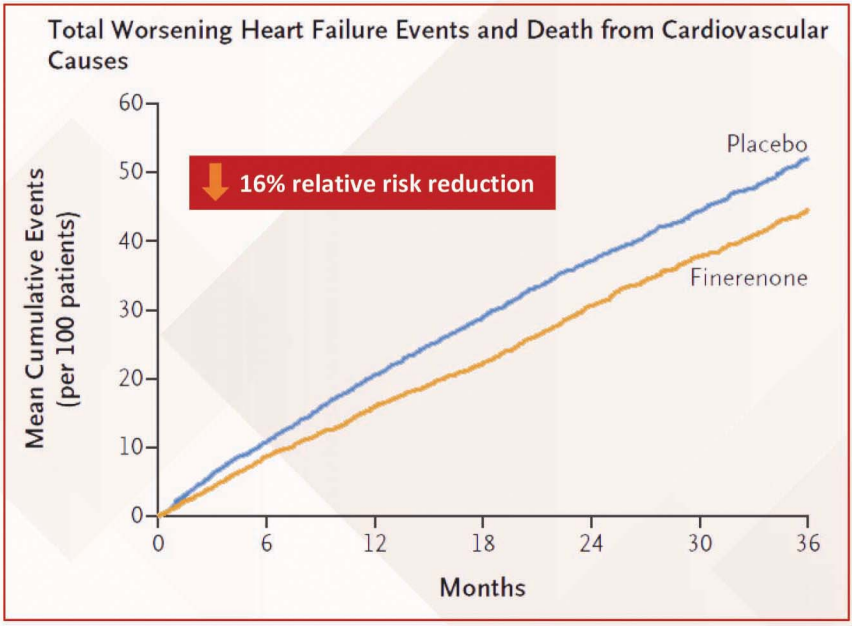


- 22 % Reduction in Hospitalization for Heart Failure
- 20 % Reduction in Renal Dialysis

FIDELITY: Conclusion - Finerenone reduced the risk of clinically important cardiovascular and kidney outcomes vs. placebo across the spectrum of CKD in patients with type 2 diabetes [10].

FINEARTS-HF Clinical Trials [11]

FINEARTS-HF



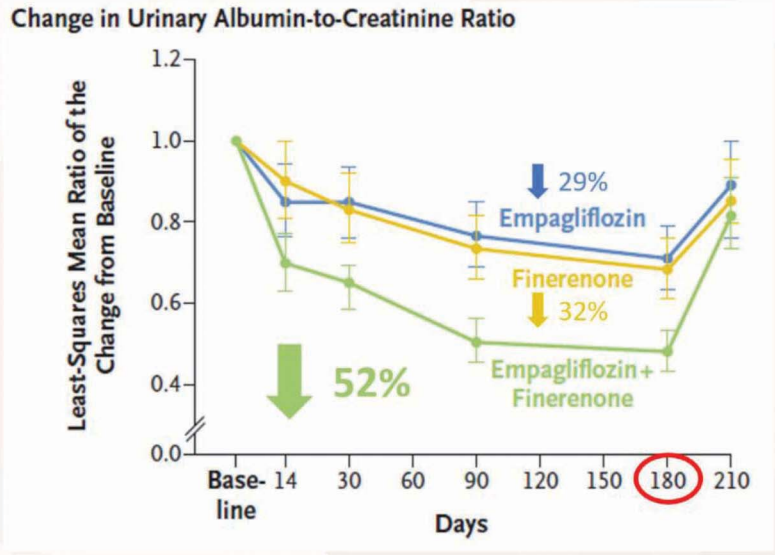
ACE=angiotensin-converting enzyme; ARB=angiotensin receptor blocker; CKD=chronic kidney disease; CV=cardiovascular; CVD=cardiovascular disease; eGFR=estimated glomerular filtration rate; MRA=mineralocorticoid receptor antagonist; T2D=type 2 diabetes; UACR=urine albumin-to-creatinine ratio.

FINEHEART Trials [12]

Pooling data in the FINE-HEART program increased precision to robustly assess the efficacy and safety of the non-steroidal MRA finerenone on important cardio-kidney outcomes and is enriched for participants with a high burden of CKM multimorbidity.

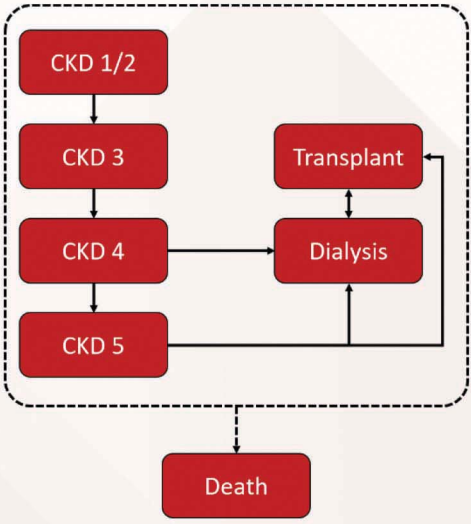
CONFIDENCE Trial [13]

CONFIDENCE: COmbinatioN effect of FInerenone anD EmpaglifloziN in participants with chronic kidney disease and type 2 diabetes using a UACR Endpoint trial



Conclusion: After 180 days, the urinary albumin-to-creatinine ratio was reduced by 52% with combination therapy, whereas 29% and 32% reduction with empagliflozin and finerenone alone respectively.

FINE-CKD: Economic value of finerenone in patients with CKD and T2D [14]



FIDELIO-DKD
18% CKD progression
14% CV event

FIGARO-DKD
13% CKD progression
13% CV event

FIDELITY
23% CKD progression
14% CV event

FINEARTS-HF
14% CV Event

- Cost Effectiveness
- Reduce Disease Burden
- Improve Quality of Life

CLINICAL GUIDELINES

Guidelines recommend Finerenone for the management of CKD associated with T2D

AMERICAN DIABETES ASSOCIATION [15] 2024

In people with type 2 diabetes and CKD with albuminuria treated with maximum tolerated doses of ACE inhibitor or ARB, addition of finerenone should be considered to improve cardiovascular outcomes and reduce the risk of CKD progression

KIDNEY DISEASE: IMPROVING GLOBAL OUTCOMES [16] 2024

Suggest a nonsteroidal mineralocorticoid receptor antagonist with proven kidney or cardiovascular benefit for adults with T2D, an eGFR ≥25 mL/min/1.73 m2, normal serum potassium concentration, and albuminuria...despite maximum tolerated dose of RAS inhibitor (RASi)

Consensus Report: AMERICAN DIABETES ASSOCIATION AND KIDNEY DISEASE: IMPROVING GLOBAL OUTCOMES [16] 2024

A nonsteroidal MRA (ns-MRA) with proven kidney and CV benefit is recommended for patients with T2D, eGFR ≥25 mL/min/1.73 m2, normal serum potassium concentration, and albuminuria (albumin-to-creatinine ratio (ACR) ≥30 mg/g) despite maximum tolerated dose of renin-angiotensin system (RAS) inhibitor.

AMERICAN ASSOCIATION OF ENDOCRINOLOGY [16] 2024

A nonsteroidal mineralocorticoid receptor antagonist (finerenone) is recommended for persons with T2D, an eGFR ≥25 mL/min/1.73 m2, normal serum potassium concentration, and albuminuria (UACR ≥30mg/g) despite a maximum tolerated dose of a renin-angiotensin system inhibitor

AMERICAN HEART ASSOCIATION [16] 2024

Finerenone can be initiated on background SGLT2 inhibitor therapy for those with eGFR >25 mL/min/1.73 m2 and potassium <5 mEq/L. Finerenone can be considered to reduce adverse cardiovascular and kidney events in Patients with diabetes and CKD already on maximally tolerated renin-angiotensin system inhibition, with or without SGLT2 inhibitor user

Guidelines recommend Finerenone to reduce Cardiovascular Risk

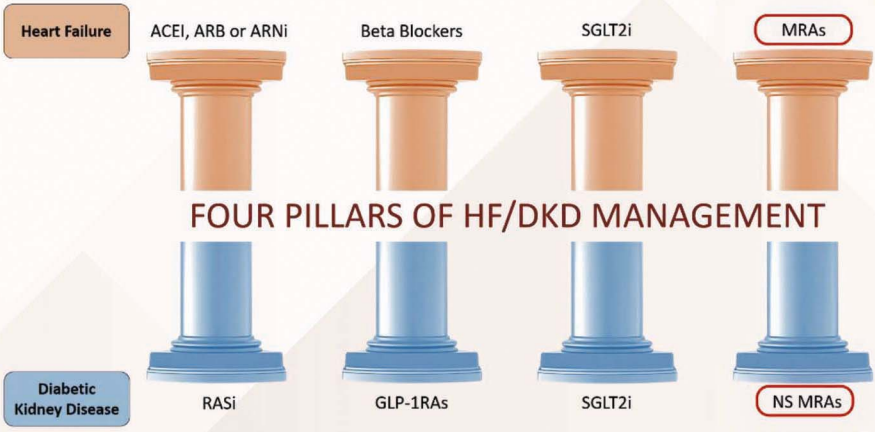
AMERICAN DIABETES ASSOCIATION [15] 2024

Individuals with T2D and diabetic kidney disease, finerenone is recommended to reduce the risk of hospitalization for heart failure

EUROPEAN SOCIETY OF CARDIOLOGY [16] 2024

Finerenone is recommended in addition to an ACEi or ARB in patients with T2DM and eGFR >60 mL/min/1.73 m2 with a UACR ≥30 mg/mmol (≥300 mg/g), or eGFR 25-60 mL/min/1.73 m2 and UACR ≥3 mg/mmol (≥30 mg/g) to reduce (the risk of) CV events and kidney failure

Four Pillars of Heart Failure and Diabetes Kidney Disease Management



Non-steroidal mineralocorticoid receptor antagonist (Finerenone) is one of the treatment options in Four Pillars of Diabetic Kidney Disease Management Guideline.

Finerenone: Clinically proven positive outcome in HFmr/p EF patients (Fulfill unmet need with steroidal MRAs)

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; MRA = mineralocorticoid receptor antagonist; T2D = type 2 diabetes; UACR = urine albumin-to-creatinine ratio.

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FINERON

Brand Name	: Fineron
Generic Name	: Finerenone
Dosage Forms and Strengths	: 10 mg, 20 mg Tablets
Route of Administration	: Oral
Pharmacologic Class	: Non-steroidal Mineralocorticoid Receptor Antagonist

QR Code for Reference Bank

Zifam

Caring For Wellbeing

- Proudly Made in Myanmar
- Trusted Quality
- Assures Availability & Affordability