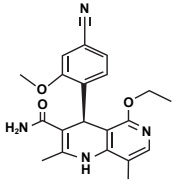
Finone™
(Finerenone)

فینون

Film-coated Tablets
10mg & 20mg

DESCRIPTION
Finone contains Finerenone, a nonsteroidal mineralocorticoid receptor antagonist. Its chemical name is (4S) 4-(4-cyano-2- methoxyphenyl)-5-ethoxy-2, 8-dimethyl-1, 4-dihydro-1, 6-naphthyridine-3-carboxamide. Its molecular formula is $C_{21}H_{22}N_4O_3$ and the structural formula is:



Finerenone

QUALITATIVE AND QUANTITATIVE COMPOSITION
Finone (Finerenone) Tablets are available for oral administration as:

Finone Tablets 10mg
Each film-coated tablet contains:
Finerenone…10mg

Finone Tablets 20mg
Each film-coated tablet contains:
Finerenone...20mg

CLINICAL PHARMACOLOGY
Mechanism 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. It's binding to 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.

Pharmacokinetics
Absorption
Finerenone exposure increased proportionally over a dose range of 1.25 to 80mg (0.06 to 4 times the maximum approved recommended dosage). Steady state of Finerenone was achieved after 2 days of dosing. The estimated steady-state geometric mean $C_{max,ss}$ was 160µg/L and steady-state geometric mean $AUC_{\tau,ss}$ was 686µg/L following administration of Finerenone 20mg to patients. Finerenone is completely absorbed after oral administration but undergoes metabolism resulting in absolute bioavailability of 44%. Finerenone C_{max} was achieved between 0.5 and 1.25 hours after dosing.

Distribution
The volume of distribution at steady-state (V_{ss}) of Finerenone is 52.6 L. Plasma protein binding of Finerenone is 92%, primarily to serum albumin, in-vitro.

Metabolism
Finerenone is primarily metabolized by CYP3A4 (90%) and to a lesser extent by CYP2C8 (10%) to inactive metabolites.

Elimination
The terminal half-life of Finerenone is about 2 to 3 hours, and the systemic blood clearance is about 25L/h. About 80% of the administered dose is excreted in urine (< 1% as unchanged) and approximately 20% in feces (<0.2% as unchanged)

Special Population
Patients with Renal Impairment
There were no clinically relevant differences in Finerenone AUC or C_{max} values in patients with eGFR 15 to < 90mL/min/1.73m^2 compared to eGFR ≥ 90mL/min/1.73m^2.

Patients with Hepatic Impairment
There was no clinically significant effect on Finerenone exposure in cirrhotic patients with mild hepatic impairment (Child Pugh A). Finerenone mean AUC was increased by 38% and C_{max} was unchanged in cirrhotic patients with moderate hepatic impairment (Child Pugh B) compared to healthy control subjects. The effect of severe hepatic impairment (Child Pugh C) on Finerenone exposure was not studied.

Elderly Patients
Elderly subjects (≥65 years of age) exhibited higher Finerenone plasma concentrations than younger subjects (≤45 years of age), with mean AUC and C_{max} values being 34% and 51% higher in the elderly.

THERAPEUTIC INDICATIONS
Finone (Finerenone) 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).

DOSAGE AND ADMINISTRATION
Prior to Initiation of Finone (Finerenone)
Measure serum potassium levels and estimated glomerular filtration rate (eGFR) before initiation. Do not initiate treatment if serum potassium is >5.0mEq/L.

Recommended Starting Dosage
The recommended starting dose of Finone (Finerenone) is based on eGFR and is presented in table below:

Recommended Starting Dosage

eGFR (mL/min/1.73m^2)	Starting Dose
≥ 60	20mg once daily
≥ 25 to < 60	10mg once daily
< 25	Not Recommended

Finone tablets may be taken with a glass of water. For patients who are unable to swallow whole tablets, Finone (Finerenone) may be crushed and mixed with water or soft foods such as applesauce immediately prior to use and administered orally.

Monitoring and Dose Adjustment
The target daily dose of Finone (Finerenone) is 20mg.
Measure serum potassium 4 weeks after initiating treatment and adjust dose (see Table below); if serum potassium levels are > 4.8 to 5.0mEq/L, initiation of Finone (Finerenone) 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.

Dose Adjustment Based on Current Serum Potassium Concentration and Current Dose

		Current Finone (Finerenone) Dose	
		10mg once daily	**20mg once daily**
Current Serum Potassium (mEq/L)	**≤ 4.8**	Increase the dose to 20mg once daily.*	Maintain 20mg once daily.
	> 4.8 – 5.5	Maintain 10mg once daily.	Maintain 20mg once daily.
	> 5.5	Withhold Finone (Finerenone). Consider restarting at 10mg once daily when serum potassium ≤ 5.0mEq/L.	Withhold Finone (Finerenone). Restart at 10mg once daily when serum potassium ≤ 5.0mEq/L.

*If eGFR has decreased by more than 30% compared to previous measurement, maintain 10mg dose.

Missed doses
Direct a patient to take a missed dose as soon as possible after it is noticed, but only on the same day. If this is not possible, the patient should skip the dose and continue with the next dose as prescribed.

Pediatric Use
The safety and efficacy of Finerenone have not been established in patients under 18 years of age. Therefore, Finerenone is not recommended for use in pediatric patients.

ADVERSE REACTIONS
Very common: Hyperkalemia.

Common: Hyponatremia, hyperuricemia, hypotension, glomerular filtration rate decreased.

Uncommon: Hemoglobin decreased.

"To report SUSPECTED ADVERSE REACTIONS to Getz Pharma's Pharmacovigilance Section, please contact at dsafety@getzpharma.com or +92-21-38636363"

CONTRAINDICATIONS
Finerenone is contraindicated in patients:
- With hypersensitivity to the active substance or to any of the excipient of the product.
- Who are receiving concomitant treatment with strong CYP3A4 inhibitors (e.g.; itraconazole, ketoconazole, ritonavir, nelfinavir, cobicistat, clarithromycin, telithromycin and nefazodone).
- With adrenal insufficiency.
- Addison's disease.

PRECAUTIONS
Hyperkalemia
Finerenone 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 Finerenone and dose accordingly. Do not initiate Finerenone if serum potassium is > 5.0 mEq/L. Measure serum potassium periodically during treatment with Finerenone and adjust dose accordingly. More frequent monitoring may be necessary for patients at risk for hyperkalemia, including those on concomitant medications that impair potassium excretion or increase serum potassium.

Concomitant medications
The risk of hyperkalemia also may increase with the intake of concomitant medications that may increase serum potassium.

Avoid concomitant use of Finerenone with the following medications:
- potassium-sparing diuretics (e.g., amiloride, triamterene)
- Other mineralocorticoid receptor antagonists (MRAs) (e.g., eplerenone, spironolactone, esaxerenone and canrenone).

Use Finerenone with caution and monitor serum potassium when taken concomitantly with the following medications:
- Potassium supplements
- Trimethoprim or trimethoprim-sulfamethoxazole. Temporary discontinuation of Finerenone may be necessary.

Use in Hepatic Impairment
Patients with severe hepatic impairment (Child Pugh C) have not been studied. Due to an expected significant increase in Finerenone exposure, avoid use of Finerenone in patients with severe hepatic impairment. Due to an increase in Finerenone exposure, consider additional serum potassium monitoring and adapt monitoring according to patient characteristics in patients with moderate hepatic impairment (Child Pugh B).

Use in Renal Impairment
The risk of hyperkalemia increases with decreasing renal function. Ongoing monitoring of renal function should be performed as needed according to standard practice. Initiation of Finerenone treatment is not recommended in patients with eGFR < 25 mL/min/1.73m^2 as clinical experience is limited. Continue Finerenone treatment with caution regarding serum potassium levels in patients with end-stage renal disease (eGFR < 15 mL/min/1.73m^2) as clinical experience is limited.

Excipients
This medication contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Pregnancy
Finerenone should not be used during pregnancy unless there has been careful consideration of the benefit for the mother and the risk to the fetus. If the patient becomes pregnant while taking Finerenone, the patient should be informed of potential risks to the fetus. Advise women of childbearing potential to use effective contraception during treatment with Finerenone.

Nursing Mothers
There are no data on the presence of Finerenone or its metabolite in human milk, the effects on the breastfed infant or the effects of the drug on milk production. Because of the potential risk to breastfed infants from exposure to Finerenone, avoid breastfeeding during treatment and for 1 day after treatment.

DRUG INTERACTIONS
Strong CYP3A4 Inhibitors
Finerenone is a CYP3A4 substrate. Concomitant use with a strong CYP3A4 inhibitor increases Finerenone exposure, which may increase the risk of Finerenone adverse reactions. Concomitant use of Finerenone with strong CYP3A4 inhibitors is contraindicated.

Moderate and Weak CYP3A4 Inhibitors
Finerenone is a CYP3A4 substrate. Concomitant use with a moderate or weak CYP3A4 inhibitor increases Finerenone exposure, which may increase the risk of Finerenone adverse reactions. Monitor serum potassium during drug initiation or dosage adjustment of either Finerenone or the moderate or weak CYP3A4 inhibitor, and adjust Finerenone dosage as appropriate.

Strong and Moderate CYP3A4 Inducers
Finerenone is a CYP3A4 substrate. Concomitant use of Finerenone with a strong or moderate CYP3A4 inducer decreases Finerenone exposure, which may reduce the efficacy of Finerenone. Avoid concomitant use of Finerenone with strong or moderate CYP3A4 inducers.

Grapefruit
Concomitant intake of grapefruit or grapefruit juice is expected to increase the plasma concentration of Finerenone and should be avoided.

Antihypertensive medicinal products
The risk for hypotension increases with concomitant use of multiple other antihypertensive medicinal products. In these patients, blood pressure monitoring is recommended.

OVERDOSAGE
In the event of suspected overdose, immediately interrupt Finerenone treatment. The most likely manifestation of overdose is hyperkalemia. If hyperkalemia develops, standard treatment should be initiated.
Finerenone is unlikely to be efficiently removed by hemodialysis given its fraction bound to plasma proteins of about 90%.

STORAGE
Do not store above 30°C.
Protect from sunlight and moisture.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
Finone (Finerenone) Tablets 10mg are available in blister pack of 20's.
Finone (Finerenone) Tablets 20mg are available in blister pack of 20's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:
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PAK-200020017