Summary of Product Characteristics

1. Name of the medicinal product

Finerenone Tablets 20 mg

Nephix 20mg Tablet

2. Qualitative and quantitative composition

Finerenone 20mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

Light Peach to Peach round shape biconvex film coated tablets, plain on both sides.

4. Clinical particulars

4.1 Therapeutic indications

Finerenone is indicated for the treatment of chronic kidney disease (stage 3 and 4 with albuminuria) associated with type 2 diabetes in adults.

4.2 Posology and method of administration

Posology

The recommended target dose is 20 mg finerenone once daily.

The maximum recommended dose is 20 mg finerenone once daily.

Initiation of treatment

Serum potassium and estimated glomerular filtration rate (eGFR) have to be measured to determine if finerenone treatment can be initiated and to determine the starting dose.

If serum potassium ≤ 4.8 mmol/L, finerenone treatment can be initiated. For monitoring of serum potassium, see below 'Continuation of treatment.'

If serum potassium > 4.8 to 5.0 mmol/L, initiation of finerenone treatment may be considered with additional serum potassium monitoring within the first 4 weeks based on patient characteristics

and serum potassium levels.

If serum potassium > 5.0 mmol/L, finerenone treatment should not be initiated.
The recommended starting dose of finerenone is based on eGFR and is presented in table 1.

Table 1: Initiation of finerenone treatment and recommended dose

eGFR (mL/min/1.73 m2)	**Starting dose (once daily)**
≥ 60	20 mg
≥ 25 to < 60	10 mg
< 25	Not recommended

Continuation of treatment
Serum potassium and eGFR have to be remeasured 4 weeks after initiation or re-start of finerenone treatment or increase in dose (see table 2 to determine continuation of finerenone treatment and dose adjustment).
Thereafter, serum potassium has to be remeasured periodically and as needed based on patient characteristics and serum potassium levels.

Table 2: **Continuation of Finerenone treatment and dose adjustment maintain 10 mg once daily, if eGFR has decreased > 30% compared to the previous measurement**

		Current Finerenone dose (once daily)	
		10 mg	**20 mg**
Current serum potassium (mmol/L)	**≤ 4.8**	Increase to 20 mg Finerenone once daily*	Maintain 20 mg once daily
	> 4.8 to 5.5	Maintain 10 mg once daily	Maintain 20 mg once daily
	> 5.5	Withhold Finerenone. Consider re-starting at 10 mg once daily when serum potassium ≤ 5.0 mmol/L.	Withhold Finerenone. Re-start at 10 mg once daily when serum potassium ≤ 5.0 mmol/L.

Missed dose

A missed dose should be taken as soon as the patient notices, but only on the same day.

The patient should not take 2 doses to make up for a missed dose.

Special populations

Elderly

No dose adjustment is necessary in elderly patients.

Renal impairment

Initiation of treatment

In patients with eGFR < 25 mL/min/1.73 m^2, finerenone treatment should not be initiated due to limited clinical data.

Continuation of treatment

In patients with eGFR ≥ 15 mL/min/1.73 m^2, finerenone treatment can be continued with dose adjustment based on serum potassium. eGFR should be measured 4 weeks after initiation to determine whether the starting dose can be increased to the recommended daily dose of 20 mg (see 'Posology, Continuation of treatment' and table 2).

Due to limited clinical data, finerenone treatment should be discontinued in patients who have progressed to end-stage renal disease (eGFR < 15 mL/min/1.73 m^2).

Hepatic impairment

Patients with

- Severe hepatic impairment:
  Finerenone should not be initiated.
- Moderate hepatic impairment:
  No initial dose adjustment is required. Consider additional serum potassium monitoring and adapt monitoring according to patient characteristics.
- Mild hepatic impairment:
  No initial dose adjustment is required.

Concomitant medication

In patients taking finerenone concomitantly with moderate or weak CYP3A4 inhibitors, potassium supplements, trimethoprim, or trimethoprim/sulfamethoxazole, additional serum potassium monitoring and adaptation of monitoring according to patient characteristics should be considered. Finerenone treatment decisions should be made as directed in table 2 ('Posology, Continuation of treatment').

Temporary discontinuation of finerenone may be necessary, when patients have to take trimethoprim, or trimethoprim/sulfamethoxazole.

Body weight

No dose adjustment is necessary based on body weight.

Paediatric population

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

Method of administration

Oral use

Tablets may be taken with a glass of water and with or without food.

Tablets should not be taken with grapefruit or grapefruit juice.

Crushing of tablets

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

4.3 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

4.4 Special warnings and precautions for use

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.

Initiation and continuation of treatment

If serum potassium > 5.0 mmol/L, finerenone treatment should not be initiated.

If serum potassium > 4.8 to 5.0 mmol/L, initiation of finerenone treatment may be considered with additional serum potassium monitoring within the first 4 weeks based on patient characteristics and serum potassium levels.

If serum potassium > 5.5 mmol/L, finerenone treatment has to be withheld. Local guidelines for the management of hyperkalaemia have to be followed.

Once serum potassium ≤ 5.0 mmol/L, finerenone treatment can be restarted at 10 mg once daily.

Monitoring

Serum potassium and eGFR have to be remeasured in all patients 4 weeks after initiation, re-start or increase in dose of finerenone. Thereafter, serum potassium has to be assessed periodically and as needed based on patient characteristics and serum potassium levels.

Concomitant medications

The risk of hyperkalaemia also may increase with the intake of concomitant medications that may increase serum potassium . See also 'Concomitant use of substances that affect finerenone exposure'.

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, canrenone.

  Finerenone should be used with caution and serum potassium should be monitored when taken concomitantly with - potassium supplements.
- Trimethoprim, or trimethoprim/sulfamethoxazole. Temporary discontinuation of finerenone may be necessary.

<u>Renal impairment</u>

The risk of hyperkalaemia increases with decreasing renal function. Ongoing monitoring of renal function should be performed as needed according to standard practice.

Initiation of treatment

Finerenone treatment should not be initiated in patients with eGFR < 25 mL/min/1.73 m^2 as clinical data are limited.

Continuation of treatment

Due to limited clinical data, finerenone treatment should be discontinued in patients who have progressed to end-stage renal disease (eGFR < 15 mL/min/1.73 m^2).

Hepatic impairment

Finerenone treatment should not be initiated in patients with severe hepatic impairment. These patients have not been studied but a significant increase in finerenone exposure is expected.

The use of finerenone in patients with moderate hepatic impairment may require additional monitoring due to an increase in finerenone exposure. Additional serum potassium monitoring and adaptation of monitoring have to be considered according to patient characteristics.

Heart failure

Patients with diagnosed heart failure with reduced ejection fraction and New York Heart Association II IV were excluded from the phase III clinical studies .

Concomitant use of substances that affect finerenone exposure

Moderate and weak CYP3A4 inhibitors

Serum potassium should be monitored during concomitant use of finerenone with moderate or weak CYP3A4 inhibitors.

Strong and moderate CYP3A4 inducers

Finerenone should not be used concomitantly with strong or moderate CYP3A4 inducers.

Grapefruit

Grapefruit or grapefruit juice should not be consumed during finerenone treatment.

Embryo-foetal toxicity

Finerenone should not be used during pregnancy unless there has been careful consideration of the benefit for the mother and the risk to the foetus. If a woman becomes pregnant while taking finerenone, she should be informed of potential risks to the foetus.

Women of childbearing potential should be advised to use effective contraception during treatment with finerenone.

Women should be advised not to breast-feed during treatment with finerenone.

Information about excipients

Finerenone contains lactose

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

Finerenone contains sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults.

Finerenone is cleared almost exclusively via cytochrome P450 (CYP)-mediated oxidative metabolism (mainly CYP3A4 [90%] with a small contribution of CYP2C8 [10%]).

Concomitant use contraindicated

Strong CYP3A4 inhibitors

Concomitant use of Finerenone with itraconazole, clarithromycin and other strong CYP3A4 inhibitors (e.g., ketoconazole, ritonavir, nelfinavir, cobicistat, telithromycin or nefazodone) is contraindicated since a marked increase in finerenone exposure is expected.

Concomitant use not recommended

Strong and moderate CYP3A4 inducers

Finerenone should not be used concomitantly with rifampicin and other strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, phenobarbital, St John's Wort) or with efavirenz and other moderate CYP3A4 inducers. These CYP3A4 inducers are expected to markedly decrease finerenone plasma concentration and result in reduced therapeutic effect.

Certain medicinal products that increase serum potassium

Finerenone should not be used concomitantly with potassium-sparing diuretics (e.g., amiloride, triamterene) and other MRAs (e.g., eplerenone, esaxerenone, spironolactone, canrenone). It is anticipated that these medicinal products increase the risk for hyperkalaemia.

Grapefruit

Grapefruit or grapefruit juice should not be consumed during finerenone treatment, as it is expected to increase the plasma concentrations of finerenone through inhibition of CYP3A4.

Concomitant use with precautions

Moderate CYP3A4 inhibitors

In a clinical study, concomitant use of erythromycin (500 mg three times a day) led to a 3.5-fold increase in finerenone AUC and 1.9-fold increase in its C_{max}. In another clinical study, verapamil (240 mg controlled-release tablet once daily) led to a 2.7- and 2.2-fold increase in finerenone AUC and C_{max}, respectively.

Serum potassium may increase, and therefore, monitoring of serum potassium is recommended, especially during initiation or changes to dosing of finerenone or the CYP3A4 inhibitor.

Weak CYP3A4 inhibitors

The physiologically based pharmacokinetic (PBPK) simulations suggest that fluvoxamine (100 mg twice daily), increases finerenone AUC (1.6-fold) and C_{max} (1.4-fold).

Serum potassium may increase, and therefore, monitoring of serum potassium is recommended, especially during initiation or changes to dosing of finerenone or the CYP3A4 inhibitor.

Certain medicinal products that increase serum potassium

Concomitant use of Finerenone with potassium supplements and trimethoprim, or trimethoprim/sulfamethoxazole is anticipated to increase the risk of hyperkalaemia. Monitoring of serum potassium is required.

Temporary discontinuation of Finerenone during trimethoprim, or trimethoprim/sulfamethoxazole treatment may be necessary.

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.

4.6 Fertility, pregnancy and lactation

Contraception in females

Women of childbearing potential should use effective contraception during finerenone treatment.

Pregnancy

There are no data from the use of finerenone in pregnant women.

Studies in animals have shown reproductive toxicity.

Finerenone should not be used during pregnancy unless the clinical condition of the woman requires treatment with finerenone. If the woman becomes pregnant while taking finerenone, she should be informed of potential risks to the foetus.

Breast-feeding

It is unknown whether finerenone/metabolites are excreted in human milk.

Available pharmacokinetic/toxicological data in animals have shown excretion of finerenone and its metabolites in milk. Rat pups exposed via this route showed adverse reactions.

A risk to the newborns/infants cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Finerenone therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

There are no data on the effect of finerenone on human fertility.

Animal studies have shown impaired female fertility at exposures considered in excess to the maximum human exposure, indicating low clinical relevance .

4.7 Effects on ability to drive and use machines

Finerenone has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reaction under treatment with finerenone was hyperkalaemia (14.0%). See 'Description of selected adverse reactions, Hyperkalaemia'.

Tabulated list of adverse reactions

The safety of finerenone in patients with chronic kidney disease (CKD) and type 2 diabetes (T2D) was evaluated in 2 pivotal phase III studies, FIDELIO-DKD (diabetic kidney disease) and FIGARO-DKD. In the FIDELIO-DKD study 2,827 patients received finerenone (10 or 20 mg once

daily) with a mean duration of treatment of 2.2 years. In the FIGARO-DKD study, 3,683 patients received finerenone (10 or 20 mg once daily) with a mean duration of treatment of 2.9 years.
The adverse reactions observed are listed in table 3. They are classified according to MedDRA`s system organ class database and frequency convention.
Adverse reactions are grouped according to their frequencies in the order of decreasing seriousness. Frequencies are defined, as follows:
Very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from the available data).

Table 3: Adverse reactions

System Organ Class (MedDRA)	**Very common**	**Common**	**Uncommon**
Metabolism and nutrition disorders	Hyperkalaemia	Hyponatraemia Hyperuricaemia	-
Vascular disorders	-	Hypotension	-
Skin and subcutaneous tissue disorders	-	Pruritus	-
Investigations	-	Glomerular filtration rate decreased	Haemoglobin decreased

Description of selected adverse reactions

Hyperkalaemia

In the pooled data of FIDELIO-DKD and FIGARO-DKD studies, hyperkalaemia events were reported in 14.0% of finerenone-treated patients compared with 6.9% of placebo-treated patients. An increase from baseline in mean serum potassium in the first month of treatment of 0.17 mmol/L was observed in the finerenone group compared to placebo, which remained stable thereafter. The

majority of hyperkalemia events were mild to moderate and resolved in patients treated with Finerenone.

Serious events of hyperkalemia were reported more frequently for Finerenone (1.1%) than for placebo (0.2%). Serum potassium concentrations > 5.5 mmol/L and > 6.0 mmol/L were reported in 16.8% and 3.3% of Finerenone-treated patients and in 7.4% and 1.2% of placebo-treated patients, respectively.

Hyperkalemia leading to permanent discontinuation in patients who received Finerenone was 1.7% versus 0.6% in the placebo group. Hospitalization due to hyperkalemia in the Finerenone group was 0.9% versus 0.2% in the placebo group.

Hypotension

In the pooled data of FIDELIO-DKD and FIGARO-DKD studies, hypotension events were reported in 4.6% of Finerenone-treated patients compared with 3.0% of placebo-treated patients. In 3 patients (< 0.1%), Finerenone treatment was permanently discontinued due to hypotension. Hospitalization due to hypotension was the same in patients receiving Finerenone or placebo (< 0.1%).

The majority of hypotension events were mild or moderate and resolved in patients treated with Finerenone. The mean systolic blood pressure decreased by 2-4 mm Hg and the mean diastolic blood pressure decreased by 1-2 mm Hg at month 1, remaining stable thereafter.

Hyperuricaemia

In the pooled data of FIDELIO-DKD and FIGARO-DKD studies, hyperuricaemia events were reported in 5.1% of Finerenone-treated patients compared with 3.9% of placebo-treated patients. All events were non-serious and did not result in permanent discontinuation in patients who received Finerenone. An increase from baseline in mean serum uric acid of 0.3 mg/dL was seen in the Finerenone group compared to placebo up to month 16, which attenuated over time. No difference between the Finerenone group and the placebo group was observed for reported events of gout (3.0%).

Glomerular filtration rate (GFR) decreased

In the pooled data of FIDELIO-DKD and FIGARO-DKD studies, GFR decreased events were reported in 5.3% of finerenone-treated patients compared with 4.2% of placebo-treated patients. GFR decreased events leading to permanent discontinuation were the same in patients receiving finerenone or placebo (0.2%). Hospitalisation due to decreased GFR was the same in patients receiving finerenone or placebo (< 0.1%).

The majority of GFR decreased events were mild or moderate and resolved in patients treated with finerenone. Patients on finerenone experienced an initial decrease in eGFR (mean 2 mL/min/1.73 m^2) that attenuated over time compared to placebo. This decrease appeared to be reversible during continuous treatment.

Haemoglobin decreased

In the pooled data of FIDELIO-DKD and FIGARO-DKD studies, finerenone was associated with a placebo-corrected absolute decrease in mean haemoglobin of 0.15 g/dL and mean haematocrit of 0.5% after 4 months of treatment. Anaemia reporting was comparable in finerenone-treated patients (6.5%) and placebo-treated patients (6.1%). The frequency of serious events of anaemia was low in both the finerenone-treated and placebo-treated patients (0.5%). Changes in haemoglobin and haematocrit were transient and reached comparable levels to those observed in the placebo-treated group after about 24-32 months.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org/

4.9 Overdose

The most likely manifestation of overdose is anticipated to be hyperkalaemia. If hyperkalaemia develops, standard treatment should be initiated.

Finerenone is unlikely to be efficiently removed by haemodialysis given its fraction bound to plasma proteins of about 90%.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: diuretics, aldosterone antagonists, ATC code: C03DA05

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. 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.

Pharmacodynamics effects

In FIDELIO-DKD and FIGARO-DKD, randomized, double-blind, placebo-controlled, multicenter phase III studies in adult patients with CKD and T2D, the placebo-corrected relative reduction in urinary albumin-to-creatinine ratio (UACR) in patients randomized to Finerenone was 31% and 32%, respectively at month 4 and UACR remained reduced throughout both studies.

In ARTS-DN, a randomized, double-blind, placebo-controlled, multicenter phase IIb study in adult patients 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.

Cardiac electrophysiology

A dedicated QT study in 57 healthy participants showed that Finerenone has no effect on cardiac repolarization. There was no indication of a QT/QTc prolonging effect of Finerenone after single doses of 20 mg (therapeutic) or 80 mg (supratherapeutic).

5.2 Pharmacokinetic properties

Absorption

Finerenone is almost completely absorbed after oral administration. Absorption is rapid with maximum plasma concentrations (C_{max}) appearing between 0.5 and 1.25 hours after tablet intake in the fasted state. The absolute bioavailability of Finerenone is 43.5% due to first-pass metabolism in the gut-wall and liver. Finerenone is a substrate of the efflux transporter P- glycoprotein in vitro,

which is however not considered relevant for its absorption in vivo due to the high permeability of Finerenone.

Effect of food

Intake with high fat, high calorie food increased Finerenone AUC by 21%, reduced C_{max} by 19% and prolonged the time to reach C_{max} to 2.5 hours. Since this is not considered as clinically relevant, Finerenone can be taken with or without food.

Distribution

The volume of distribution at steady state (V_{ss}) of Finerenone is 52.6 L. The human plasma protein binding of finerenone in vitro is 91.7%, with serum albumin being the main binding protein.

Biotransformation

Approximately 90% of Finerenone metabolism is mediated by CYP3A4 and 10% by CYP2C8. Four major metabolites were found in plasma. All metabolites are pharmacologically inactive.

Elimination

The elimination of finerenone from plasma is rapid with an elimination half-life ($t_{½}$) of about 2 to 3 hours. Systemic blood clearance of finerenone is about 25 L/h. About 80% of the administered dose was excreted via urine and approximately 20% of the dose was excreted via faeces. Excretion was almost exclusively in the form of metabolites, while excretion of unchanged finerenone represents a minor route (< 1% of dose in the urine due to glomerular filtration, < 0.2% in the faeces).

Linearity

Finerenone pharmacokinetics are linear across the investigated dose range from 1.25 to 80 mg given as single dose tablets.

Special populations

Elderly

Of the 2,827 patients who received finerenone in the FIDELIO-DKD study, 58% of patients were 65 years and older, and 15% were 75 years and older. Of the 3,683 patients who received finerenone in the FIGARO-DKD study, 52% of patients were 65 years and older, and 13% were 75 years and older.

In both studies, no overall differences in safety or efficacy were observed between these patients and younger patients.

In a phase I study (N = 48) elderly healthy participants (≥ 65 years of age) exhibited higher finerenone plasma concentrations than younger healthy participants (≤ 45 years of age), with mean AUC and C_{max} values being 34% and 51% higher in the elderly. Populationpharmacokinetic analyses did not identify age as a covariate for finerenone AUC or C_{max}.

Renal impairment

Mild renal impairment (creatinine clearance [CL_{CR}] 60 to < 90 mL/min) did not affect finerenone AUC and C_{max}.

Compared to patients with normal renal function (CL_{CR} ≥ 90 mL/min), the effect of moderate (CL_{CR} 30 to < 60 mL/min) or severe (CL_{CR} < 30 mL/min) renal impairment on AUC of finerenone was similar with increases by 34-36%. Moderate or severe renal impairment had no effect on C_{max}. Due to the high plasma protein binding, finerenone is not expected to be dialysable.

Hepatic impairment

There was no change in finerenone exposure in cirrhotic patients with mild hepatic impairment.

In cirrhotic patients with moderate hepatic impairment, finerenone total and unbound AUC were increased by 38% and 55%, respectively, while no change in C_{max} was observed compared to healthy control participants.

There are no data in patients with severe hepatic impairment.

Body weight

Population-pharmacokinetic analyses identified body weight as a covariate for finerenone C_{max}. The C_{max} of a subject with a body weight of 50 kg was estimated to be 38% to 51% higher compared to a subject of 100 kg. Dose adaptation based on body weight is not warranted.

<u>Pharmacokinetic/pharmacodynamic relationships</u>

The concentration-effect relationship over time for UACR was characterised by a maximum effect model indicating saturation at high exposures. The model-predicted time to reach the full (99%) steady-state drug effect on UACR was 138 days. The pharmacokinetic (PK) half-life was 2-3 hours

and PK steady state was achieved after 2 days, indicating an indirect and delayed effect on pharmacodynamic responses.

Clinical studies with no relevant drug-drug interactions

Concomitant use of gemfibrozil (600 mg twice daily), a strong inhibitor of CYP2C8, increased finerenone mean AUC and C_{max} 1.1-fold and 1.2-fold, respectively. This is not considered as clinically relevant.

Pre- and co-treatment with the proton pump inhibitor omeprazole (40 mg once daily) had no effect on finerenone mean AUC and mean C_{max}.

Concomitant use of antacid aluminium hydroxide and magnesium hydroxide (70 mVal) had no effect on finerenone mean AUC and reduced its mean C_{max} by 19%. This is not considered as clinically relevant.

In vivo a multiple-dose regimen of 20 mg finerenone given once daily for 10 days had no relevant effect on the AUC of the CYP3A4 probe substrate midazolam. Therefore, a clinically relevant inhibition or induction of CYP3A4 by finerenone can be excluded.

A single dose of 20 mg finerenone also had no clinically relevant effect on AUC and C_{max} of the CYP2C8 probe substrate repaglinide. Thus, finerenone does not inhibit CYP2C8.

Lack of mutual pharmacokinetic interaction was demonstrated between finerenone and the CYP2C9 substrate warfarin and between finerenone and the P-gp substrate digoxin.

Multiple doses of 40 mg finerenone once daily had no clinically relevant effect on AUC and C_{max} of the breast cancer resistance protein (BCRP) and organic anion transporting polypeptides (OATP) substrate rosuvastatin.

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, single dose toxicity, repeated dose toxicity, genotoxicity, phototoxicity, carcinogenic potential and male and female fertility.

Repeated dose toxicity

In dogs, a reduced prostate weight and size was found at an $AUC_{unbound}$ of about 10 to 60 times that in humans. The dose free of findings provides a safety margin of about 2.

Carcinogenic potential

In 2-year carcinogenicity studies, finerenone did not show carcinogenic potential in male and female rats or female mice. In male mice, finerenone resulted in an increase in Leydig cell adenoma at doses representing 26 times the $AUC_{unbound}$ in humans. A dose representing 17 times the $AUC_{unbound}$ in humans did not cause any tumours. Based on the known sensitivity of rodents to develop these tumours and the pharmacology-based mechanism at supratherapeutic doses as well as adequate safety margins, the increase in Leydig cell tumours in male mice is not clinically relevant.

Toxicity to development

In the embryo-foetal toxicity study in rats, finerenone resulted in reduced placental weights and signs of foetal toxicity, including reduced foetal weights and retarded ossification at the maternal toxic dose of 10 mg/kg/day corresponding to an $AUC_{unbound}$ of 19 times that in humans. At 30 mg/kg/day, the incidence of visceral and skeletal variations was increased (slight oedema, shortened umbilical cord, slightly enlarged fontanelle) and one foetus showed complex malformations including a rare malformation (double aortic arch) at an $AUC_{unbound}$ of about 25 times that in humans. The doses free of any findings (low dose in rats, high dose in rabbits) provided safety margins of 10 to 13 times for $AUC_{unbound}$. Therefore, the findings in rats do not indicate an increased concern for foetal harm.

When rats were exposed during pregnancy and lactation in the pre- and postnatal developmental toxicity study, increased pup mortality and other adverse effects (lower pup weight, delayed pinna unfolding) were observed at about 4 times the $AUC_{unbound}$ expected in humans. In addition, the offspring showed slightly increased locomotor activity, but no other neurobehavioural changes starting at about 4 times the $AUC_{unbound}$ expected in humans. The dose free of findings provided a safety margin of about 2 for $AUC_{unbound}$. The increased locomotor activity in offspring may indicate a potential risk for the foetus. In addition, because of the findings in pups, a risk for the nursing newborn/infant cannot be excluded.

Female fertility

Finerenone caused reduced female fertility (decreased number of corpora lutea and implantation sites) as well as signs of early embryonic toxicity (increased post-implantational loss and decreased

number of viable foetuses) at about 21 times the human $AUC_{unbound}$. In addition, reduced ovarian weights were found at about 17 times the human $AUC_{unbound}$. No effects on female fertility and early embryonic development were found at 10 times the human $AUC_{unbound}$. Therefore, the findings in female rats are of little clinical relevance.

6. Pharmaceutical particulars

6.1 List of excipients

Micro Crystalline Cellulose PH 101

Lactose Monohydrate

Cross Carmellose sodium

Magnesium stearate

Micro Crystalline Cellulose PH 102

Sodium Lauryl Sulfate

Colloidal Anhydrous Silica (Aerosil)

Readycoat film Aq Peach

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 30°C. Protect from direct sunlight. Keep all medicines out of reach of children.

6.5 Nature and contents of container

3 X 10 Alu Alu Tablets

6.6 Special precautions for disposal and other handling

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. **Marketing authorisation holder**

   DAWA LIMITED

   Baba Dogo Road, Ruaraka,

   P.O.Box 16633-00620

   Nairobi, Kenya

8. **Marketing authorisation number(s)**

   H2025/CTD12130/26334

9. **Manufacturer Name:**

   Cubit Lifesciences LLP

   Plot No. 39-40, Ozone Industrial Park, At. & post:

   Kerala- Bhayla Near. Kerala G.I.D.C,

   Taluka: Bavla, Dist.: Ahmedabad–382220 Gujarat India.

10. **Date of first authorisation/renewal of the authorisation**

    August 2025

11. **Date of revision of the text**

    Not Applicable