SUMMARY PRODUCT CHARACTERISTICS

1.NAME OF THE MEDICINAL PRODUCT

Nephix 10 mg Tablets

2.QUALITATIVE AND QUANTITATIVE COMPOSITION

Nephix 10 mg film-coated tablets
Each film-coated tablet contains Finerenone$_{10mg}$

Excipient with known effect: Lactose monohydrate
For the full list of excipients, section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet
Nephix 10 mg film-coated tablets
Light Peach to Peach round shape biconvex film coated tablets, plain on both sides

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Nephix 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 Finerenone 20 mg once daily.
The maximum recommended dose is Finerenone 20 mg 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.

eGFR (mL/min/1.73 $m^{2)}$	Starting dose (once daily)

≥ 60	20 mg
≥ 25 to < 60	10 mg
< 25	Not recommended

Serum Potassium and eGFR have to be remeasured 4 weeks after initiation or re-start of finerenone treatment or increase in dose (As per table 2 below 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

		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.

* Maintain 10 mg once daily, if eGFR has decreased > 30% compared to the previous measurement

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.

Renal impairment

Initiation of treatment

In patients with eGFR < 25 mL/min/1.73 m2, Finerenone treatment should not be initiated due to limited clinical data.

Continuation of treatment

In patients with eGFR ≥ 15 mL/min/1.73 m2, 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 20mg ('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 m2).

Hepatic impairment

Patients with

-Severe hepatic impairment:

Finerenone should not be initiated. No data are available.
-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, Nephix tablets may be crushed and mixed with water or soft foods, such as apple sauce, directly before oral use.

4.3 Contraindications 4.4 Special warnings and precautions for use

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Hyperkalaemia

Hyperkalaemia has been observed in patients treated withFinerenone Some patients are at a higher risk to develop hyperkalaemia.

Risk factors include low eGFR, higher serum Potassium and previous episodes of hyperkalaemia. 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.

Renal impairment

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 m2 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 m2).

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

Nephix contains lactose

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

Nephix 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 Nephix 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

Nephix 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

Nephix 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 controlledrelease 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 Nephix a 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 Nephix 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.
Nephix 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 Nephix 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

Nephix 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' below.

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 hyperkalaemia events were mild to moderate and resolved in patients treated with finerenone.

Serious events of hyperkalaemia 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.

Hyperkalaemia leading to permanent discontinuation in patients who received finerenone was 1.7% versus

0.6% in the placebo group. Hospitalisation due to hyperkalaemia in the finerenone group was 0.9% versus

0.2% in the placebo group.

For specific recommendations,

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. Hospitalisation 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 m2) 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 hemoglobin and hematocrit were transient and reached comparable levels to those observed in the placebo-treated group after about 24-32 months. **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.
Pharmacodynamic effects

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

In ARTS-DN, a randomised, double-blind, placebo-controlled, multicentre 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 repolarisation. There was no indication of a QT/QTc prolonging effect of finerenone after single doses of 20 mg (therapeutic) or 80 mg (supratherapeutic).

Clinical efficacy and safety

The FIDELIO-DKD and FIGARO-DKD studies investigated the effect of finerenone compared to placebo on kidney and cardiovascular (CV) outcomes in adult patients with CKD and T2D.

Patients were required to be receiving standard of care, including a maximum tolerated labelled dose of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB).

Patients with diagnosed heart failure with reduced ejection fraction and New York Heart Association II-IV were excluded due to the class 1A recommendation for MRA therapy.

In the FIDELIO-DKD study patients were eligible based on evidence of persistent albuminuria (> 30 mg/g

to 5,000 mg/g), an eGFR of 25 to 75 mL/min/1.73 m2 and serum potassium ≤ 4.8 mmol/L at screening. The primary endpoint was a composite of time to first occurrence of kidney failure (defined as chronic dialysis or kidney transplantation, or a sustained decrease in eGFR to < 15 mL/min/1.73 m2 over at least 4 weeks), a sustained decline in eGFR of 40% or more compared to baseline over at least 4 weeks, or renal death. The key secondary endpoint was a composite of time to first occurrence of CV death, non-fatal myocardial infarction (MI), non-fatal stroke or hospitalisation for heart failure.

A total of 5,674 patients were randomised to receive either finerenone (N = 2,833) or placebo (N = 2,841) and included in the analyses. The median follow-up was 2.6 years. The dose of finerenone or placebo could be adjusted between 10 mg and 20 mg once daily during the course of the study, based mainly on serum potassium concentration. At month 24, of the subjects

treated with finerenone, 67% were treated with 20 mg once daily, 30% with 10 mg once daily and 3% were on a treatment interruption.

After the end of study, vital status was obtained for 99.7% of patients. The study population was 63% White, 25% Asian and 5% Black. The mean age at enrolment was 66 years and 70% of patients were male. At baseline, the mean eGFR was 44.3 mL/min/1.73 m2, with 55% of patients having an eGFR < 45 mL/min/1.73 m2, median UACR was 852 mg/g, and mean HbA1c was 7.7%, 46% had a history of atherosclerotic CV disease, 30% a history of coronary artery disease, 8% a history of cardiac failure, and the mean blood pressure was 138/76 mm Hg. The mean duration of T2D at baseline was 16.6 years and a history of diabetic retinopathy and diabetic neuropathy was reported in 47% and 26% of patients, respectively. At baseline, almost all patients were on ACEi (34%) or ARB (66%), and 97% of patients used one or more antidiabetic medications (insulin [64%], biguanides [44%], glucagon-like peptide-1 [GLP-1] receptor agonists [7%], sodium-glucose cotransporter 2 [SGLT2] inhibitors [5%]). The other most frequent medications taken at baseline were statins (74%) and calcium channel blockers (63%).

A statistically significant difference in favour of finerenone was shown for the primary composite endpoint and the key secondary composite endpoint (see figure 1/table 4 below). The treatment effect for the primary and key secondary endpoints was generally consistent across subgroups, including region, eGFR, UACR, systolic blood pressure (SBP) and HbA1c at baseline.

In the FIGARO-DKD study patients were eligible, based on evidence of persistent albuminuria having an UACR of ≥ 30 mg/g to < 300 mg/g and an eGFR of 25 to 90 mL/min/1.73 m2, or an UACR ≥ 300 mg/g and an eGFR ≥ 60 mL/min/1.73 m2 at screening. Patients were required to have a serum potassium of ≤ 4.8 mmol/L at screening.

The primary endpoint was a composite of time to first occurrence of CV death, non-fatal MI, non-fatal stroke or hospitalisation for heart failure. The secondary endpoint was 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 randomised to receive either finerenone (N = 3,686), or placebo (N = 3,666) and included in the analyses. The median follow-up was 3.4 years. The dose of finerenone or placebo could be adjusted between 10 mg and 20 mg once daily during the course of the study, based mainly on serum potassium concentration. At month 24, of the subjects treated with finerenone, 82% were treated with 20 mg once daily, 15% with 10 mg once daily and 3% were on a treatment interruption. After the end of study, vital status was obtained for 99.8% of patients. The study population was 72% White, 20% Asian and 4% Black. The mean age at

enrolment was 64 years and 69% of patients were male. 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 UACR was 308 mg/g, and mean HbA1c was 7.7%, 45% of patients had a history of atherosclerotic CV disease, 8% had a history of cardiac failure, and the mean blood pressure was 136/77 mm Hg. The mean duration of T2D at baseline was 14.5 years and a history of diabetic retinopathy and diabetic neuropathy was reported in 31% and 28% of patients, respectively. At baseline, almost all patients were on ACEi (43%) or ARB (57%), and 98% of patients used one or more antidiabetic medications (insulin [54%], biguanides [69%], GLP-1 receptor agonists [7%], SGLT2 inhibitors [8%]). The other most frequent medication taken at baseline was statins (71 %).A statistically significant difference in favour of finerenone was shown for the CV primary composite endpoint (see figure 2/table 5 below). The treatment effect for the primary endpoint was consistent across subgroups, including region, eGFR, UACR, SBP and HbA1c at baseline.

A lower incidence rate of the secondary composite outcome of kidney failure, sustained eGFR decline of 40% or more or renal death was observed in the finerenone group compared to placebo, however this difference did not achieve statistical significance (see table 5 below). The treatment effect for the kidney secondary composite endpoint was consistent across subgroups of eGFR at baseline, but for the subgroup of patients with UACR < 300 mg/g the HR was 1.16 (95% CI 0.91; 1.47) and for the subgroup of patients with UACR ≥ 300 mg/g the HR was 0.74 (95% CI 0.62; 0.90).

Table 4: Analysis of the primary and secondary time-to-event endpoints (and their individual components) in phase III study FIDELIO-DKD

	Nephix* (N = 2,833)		Placebo (N = 2,841)		Treatment effect
	N (%)	Events/ 100-pyr	N (%)	Events/ 100-pyr	HR (95% CI)
Primary renal composite endpoint and its components					
Composite of kidney failure, sustained eGFR decline ≥ 40% or renal death	504 (17.8)	7.59	600 (21.1)	9.08	0.82 (0.73; 0.93) p = 0.0014
Kidney failure	208 (7.3)	2.99	235 (8.3)	3.39	0.87 (0.72; 1.05)
Sustained eGFR decline ≥ 40%	479 (16.9)	7.21	577 (20.3)	8.73	0.81 (0.72; 0.92)
Renal death	2 (< 0.1)	-	2 (< 0.1)	-	-
Key secondary CV composite endpoint and its components					
Composite of CV death, non-fatal MI, non-fatal stroke or	367 (13.0)	5.11	420 (14.8)	5.92	0.86 (0.75; 0.99) p = 0.0339

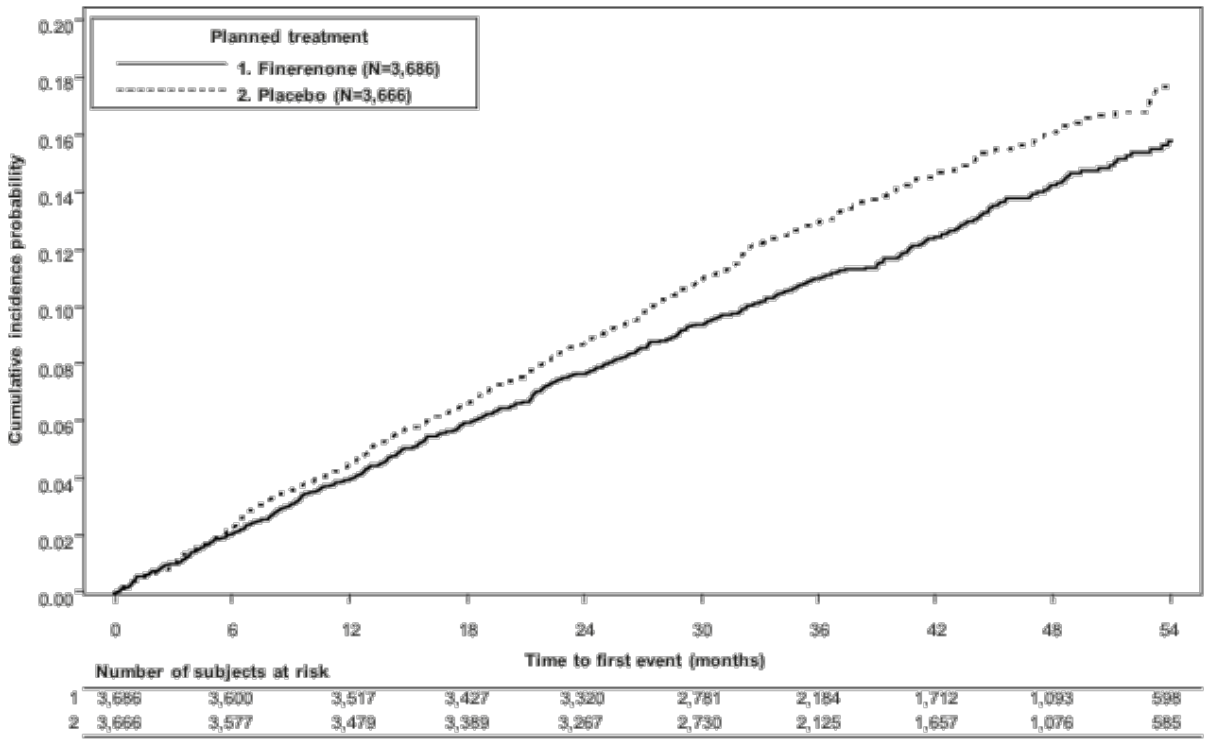
hospitalisation for heart failure					
CV death	128 (4.5)	1.69	150 (5.3)	1.99	0.86 (0.68;1.08)
Non-fatal MI	70 (2.5)	0.94	87 (3.1)	1.17	0.80 (0.58;1.09)
Non-fatal stroke	90 (3.2)	1.21	87 (3.1)	1.18	1.03 (0.76;1.38)
Hospitalisation for heart failure	139 (4.9)	1.89	162 (5.7)	2.21	0.86 (0.68;1.08)
Secondary efficacy endpoints					
All-cause mortality	219 (7.7)	2.90	244 (8.6)	3.23	0.90 (0.75; 1.07) **
All-cause hospitalisation	1,263 (44.6)	22.56	1,321 (46.5)	23.87	0.95 (0.88; 1.02) **
Composite of kidney failure, sustained eGFR decline ≥ 57% or renal death	252 (8.9)	3.64	326 (11.5)	4.74	0.76 (0.65; 0.90) **

* Treatment with 10 or 20 mg once daily in addition to maximum tolerated labelled doses of ACEi or ARB.

** p not statistically significant after adjustment for multiplicity CI: Confidence interval

HR: Hazard ratio

pyr: patient-years



Paediatric population

The licensing authority has deferred the obligation to submit the results of studies with Nephix in one or more subsets of the paediatric population in treatment of chronic kidney disease (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Finerenone is almost completely absorbed after oral administration. Absorption is rapid with maximum plasma concentrations (Cmax) 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 Cmax by 19% and prolonged the time to reach Cmax 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 (Vss) 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 (t½) 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).

5.3 Preclinical safety data
Not applicable

6. Pharmaceutical particulars
6.1 List of excipients

Cellulose, microcrystalline

Croscarmellose sodium

Hypromellose 2910

Lactose monohydrate

Magnesium stearate

Sodium lauryl sulfate

Hypromellose 2910

Titanium dioxide

Talc Iron oxide red (E 172)

6.2 Incompatibilities Not

applicable.

6.3 Shelf life
36 months from the date of manufacture

6.4 Special precautions for storage:
This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container.

Alu-Alu Blister Pack of 3x10's, packed in printed unit carton along with literature insert.

6.6 Special precautions for disposal and other handling

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

7. MARKET AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESS

Dawa Limited,

Plot No. 7879/8, Baba Dogo

Road, Ruaraka, P.O Box

16633-00620, Nairobi,

Kenya.

Manufacturer:

Cubit Lifesciences LLP

Address: Plot No. 39-40, Ozone Industrial Park,

At. & post: Kerala- Bhayla Near. Kerala

G.I.D.C, Taluka: Bavla, Dist.: Ahmedabad–

382220 Country: India.

8. MARKETING AUTHORISATION NUMBER

H2025/CTD12129/26333

8. DATE OF FIRST REGISTRATION/ RENEWAL REGISTRATION

27/08/2025

9. DATE OF REVISION OF THE TEXT

27/08/2025