ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Kerendia 10 mg film-coated tablets
Kerendia 20 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Kerendia 10 mg film-coated tablets

Each film-coated tablet contains 10 mg of finerenone.

Excipient with known effect
Each film-coated tablet contains 45 mg of lactose (as monohydrate), see section 4.4.

Kerendia 20 mg film-coated tablets

Each film-coated tablet contains 20 mg of finerenone.

Excipient with known effect
Each film-coated tablet contains 40 mg of lactose (as monohydrate), see section 4.4.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (tablet)

Kerendia 10 mg film-coated tablets

Pink, oval-oblong film-coated tablet with a length of 10 mm and a width of 5 mm, marked ‘10’ on one side and ‘FI’ on the other side.

Kerendia 20 mg film-coated tablets

Yellow, oval-oblong film-coated tablet with a length of 10 mm and a width of 5 mm, marked ‘20’ on one side and ‘FI’ on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Kerendia is indicated for the treatment of chronic kidney disease (with albuminuria) associated with type 2 diabetes in adults.
For study results with respect to renal and cardiovascular events, see section 5.1.

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 (see section 4.4).

If serum potassium > 5.0 mmol/L, finerenone treatment should not be initiated (see section 4.4).

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 m^2)	**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.
See sections 4.4 and 4.5 for more information.

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.

Special populations

Elderly
No dose adjustment is necessary in elderly patients (see section 5.2).

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 (see sections 4.4 and 5.2).

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) (see section 4.4).

Hepatic impairment
Patients with
- severe hepatic impairment:
  Finerenone should not be initiated (see sections 4.4 and 5.2). 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 (see sections 4.4 and 5.2).

- 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 (see section 4.4). 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. See sections 4.4 and 4.5 for more information.

Body weight
No dose adjustment is necessary based on body weight (see section 5.2).

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 (see section 5.2).
Tablets should not be taken with grapefruit or grapefruit juice (see section 4.5).

Crushing of tablets
For patients who are unable to swallow whole tablets, Kerendia tablets may be crushed and mixed with water or soft foods, such as apple sauce, directly before oral use (see section 5.2).

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Concomitant treatment with strong inhibitors of CYP3A4 (see section 4.5), e.g.,
  - itraconazole
  - ketoconazole
  - ritonavir
  - nelfinavir
  - cobicistat
  - clarithromycin
  - telithromycin
  - nefazodone
- Addison's disease

4.4 Special warnings and precautions for use

Hyperkalaemia

Hyperkalaemia has been observed in patients treated with finerenone (see section 4.8).
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 (*see section 4.2)*
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 (see section 4.2).

Concomitant medications
The risk of hyperkalaemia also may increase with the intake of concomitant medications that may increase serum potassium (see section 4.5.). 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 (see section 4.2).

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 (see sections 4.2 and 5.2).

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 (see section 4.2). These patients have not been studied (see section 5.2) 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 (see sections 4.2 and 5.2).

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 (see section 5.1).

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 (see sections 4.2 and 4.5).

Strong and moderate CYP3A4 inducers
Finerenone should not be used concomitantly with strong or moderate CYP3A4 inducers (see section 4.5).

Grapefruit
Grapefruit or grapefruit juice should not be consumed during finerenone treatment (see sections 4.2 and 4.5).

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.
See sections 4.6 and 5.3 for more information.

Information about excipients

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

Kerendia 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 Kerendia with itraconazole, clarithromycin and other strong CYP3A4 inhibitors (e.g., ketoconazole, ritonavir, nelfinavir, cobicistat, telithromycin or nefazodone) is contraindicated (see section 4.3), since a marked increase in finerenone exposure is expected.

Concomitant use not recommended

Strong and moderate CYP3A4 inducers
Kerendia 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 (see section 4.4).

Certain medicinal products that increase serum potassium
Kerendia 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 (see section 4.4)

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 (see sections 4.2 and 4.4).

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 (see sections 4.2 and 4.4).

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 (see sections 4.2 and 4.4).

Certain medicinal products that increase serum potassium (see section 4.4)
Concomitant use of Kerendia 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 Kerendia 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 (see section 4.4).

Pregnancy

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

Studies in animals have shown reproductive toxicity (see section 5.3).

Kerendia 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 (see section 4.4).

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 (see section 5.3).
A risk to the newborns/infants cannot be excluded.
A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Kerendia therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman (see section 4.4).

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 (see section 5.3).

4.7 Effects on ability to drive and use machines

Kerendia 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 and section 4.4.

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, refer to sections 4.2 and 4.4.

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 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 the national reporting system listed in Appendix V.

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 m^2 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 m^2 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 m^2, with 55% of patients having an eGFR < 45 mL/min/1.73 m^2, 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 m^2, or an UACR ≥ 300 mg/g and an eGFR ≥ 60 mL/min/1.73 m^2 at screening. Patients were required to have a serum potassium of ≤ 4.8 mmol/L at screening.

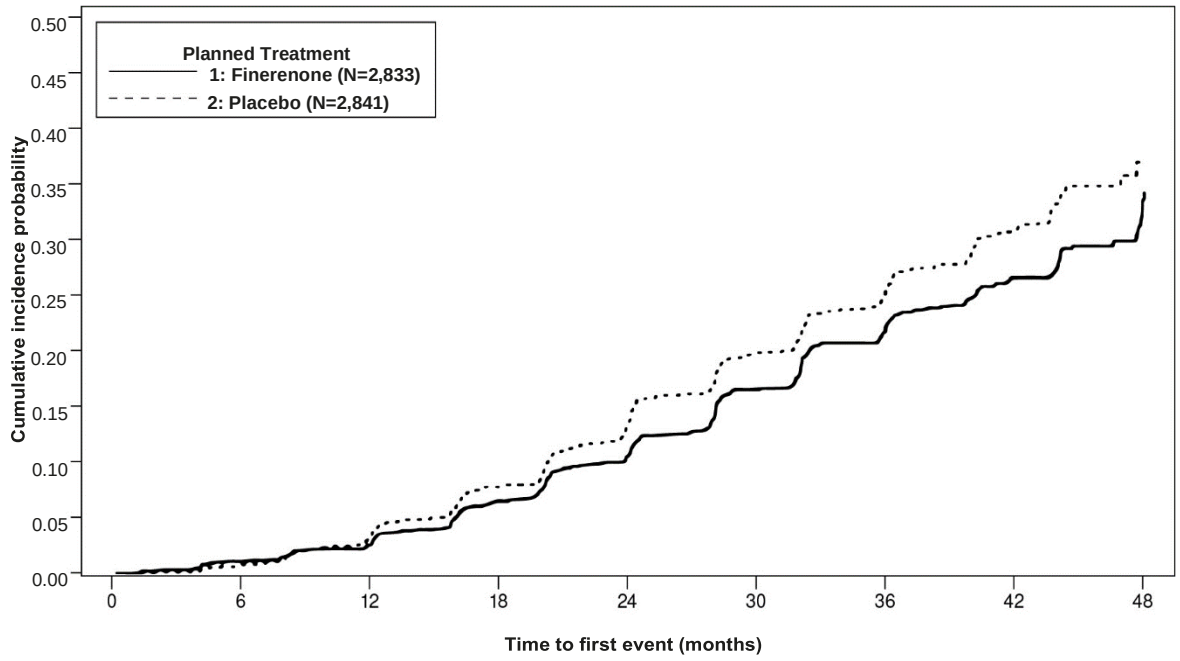
The primary endpoint was a composite of time to first occurrence of CV death, non-fatal MI, non-fatal stroke or hospitalisation for heart failure. The secondary endpoint was a composite of time to kidney failure, a sustained decline in eGFR of 40% or more compared to baseline over at least 4 weeks, or 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 m^2, with 62% of patients having an eGFR ≥ 60 mL/min/1.73 m^2, 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).
Additional prespecified secondary time-to-event endpoints are included in table 5.

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

	Kerendia* (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 hospitalisation for heart failure	367 (13.0)	5.11	420 (14.8)	5.92	0.86 (0.75; 0.99) p = 0.0339
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

Figure 1: Time to first occurrence of kidney failure, sustained decline in eGFR ≥ 40% from baseline, or renal death in the FIDELIO-DKD study



Number of subjects at risk

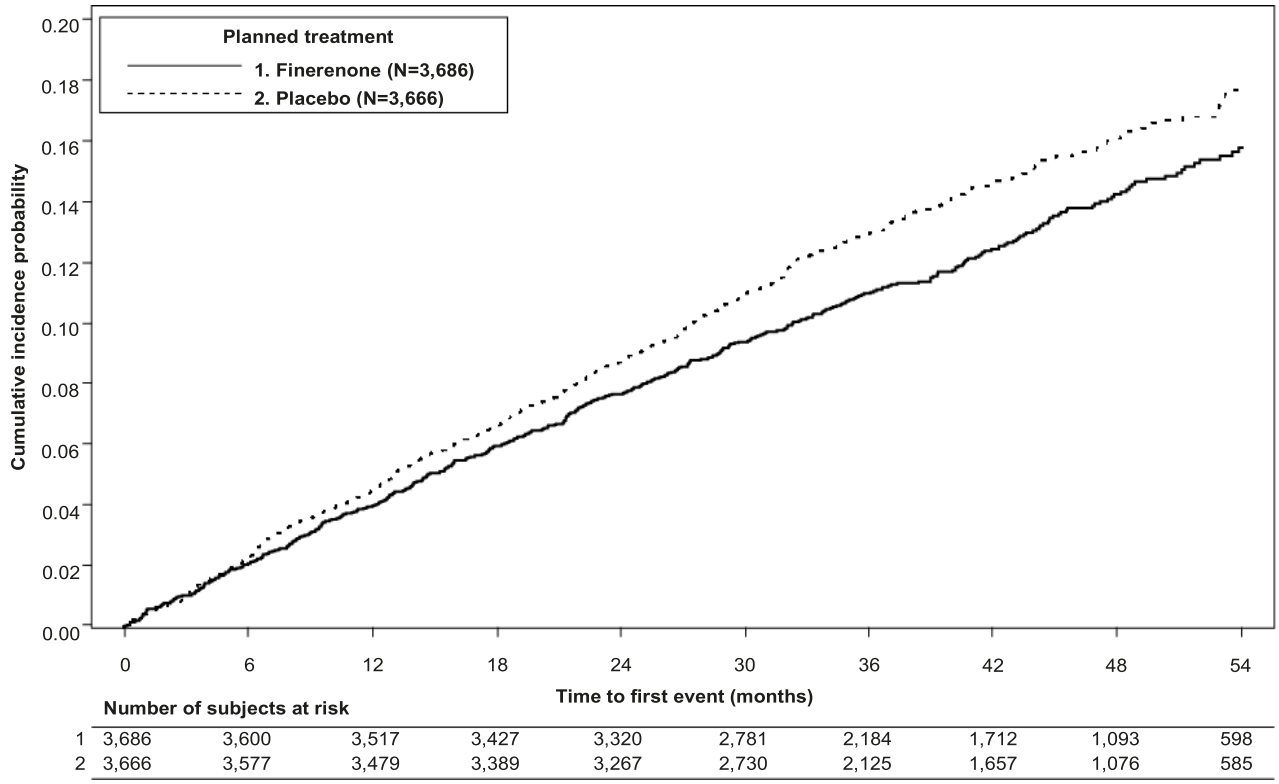
1	2,833	2,705	2,607	2,397	1,808	1,274	787	441	83
2	2,841	2,724	2,586	2,379	1,759	1,248	792	453	82

Table 5: Analysis of the primary and secondary time-to-event endpoints (and their individual components) in phase III study FIGARO-DKD

	Kerendia* (N = 3,686)		Placebo (N = 3,666)		Treatment effect
	N (%)	Events/ 100-pyr	N (%)	Events/ 100-pyr	HR (95% CI)
Primary CV composite endpoint and its components					
Composite of CV death, non-fatal MI, non-fatal stroke or hospitalisation for heart failure	458 (12.4)	3.87	519 (14.2)	4.45	0.87 (0.76; 0.98) p = 0.0264
CV death	194 (5.3)	1.56	214 (5.8)	1.74	0.90 (0.74; 1.09)
Non-fatal MI	103 (2.8)	0.85	102 (2.8)	0.85	0.99 (0.76; 1.31)
Non-fatal stroke	108 (2.9)	0.89	111 (3.0)	0.92	0.97 (0.74; 1.26)
Hospitalisation for heart failure	117 (3.2)	0.96	163 (4.4)	1.36	0.71 (0.56; 0.90)
Secondary renal composite endpoint and its components					
Composite of kidney failure, sustained eGFR decline ≥ 40% or renal death	350 (9.5)	3.15	395 (10.8)	3.58	0.87 (0.76; 1.01) p = 0.0689 **
Kidney failure	46 (1.2)	0.40	62 (1.7)	0.54	0.72 (0.49;1.05)
Sustained eGFR decline ≥ 40%	338 (9.2)	3.04	385 (10.5)	3.49	0.87 (0.75; > 1.00)
Renal death	0	-	2 (< 0.1)	-	-
Secondary efficacy endpoints					
All-cause mortality	333 (9.0)	2.68	370 (10.1)	3.01	0.89 (0.77; 1.04) **
All-cause hospitalisation	1,573 (42.7)	16.91	1,605 (43.8)	17.52	0.97 (0.90; 1.04) **
Composite of kidney failure, sustained eGFR decline ≥ 57% or renal death	108 (2.9)	0.95	139 (3.8)	1.23	0.77 (0.60; 0.99) **

* Treatment with 10 or 20 mg once daily in addition to maximum tolerated labelled doses of ACEi or ARB.
** not statistically significant after adjustment for multiplicity
CI: Confidence interval
HR: Hazard ratio
pyr: patient-years

Figure 2: Time to first occurrence of CV death, non-fatal myocardial infarction, non-fatal stroke or hospitalisation for heart failure in the FIGARO-DKD study



Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Kerendia 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 (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 (see section 4.2). Population-pharmacokinetic 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} (see section 4.2).
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 (see section 4.2).
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 (see section 4.2).
There are no data in patients with severe hepatic impairment (see sections 4.2 and 4.5).

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 (see section 4.2).

Pharmacokinetic/pharmacodynamic relationships

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.

5.3 Preclinical safety data

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 (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Cellulose, microcrystalline
Croscarmellose sodium
Hypromellose 2910
Lactose monohydrate
Magnesium stearate
Sodium laurilsulfate

Tablet coating

Hypromellose 2910
Titanium dioxide
Talc

Kerendia 10 mg film-coated tablets
Iron oxide red (E 172)

Kerendia 20 mg film-coated tablets
Iron oxide yellow (E 172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/PVDC/Aluminium transparent calendarised blisters with 14 film-coated tablets. Pack sizes of 14, 28 or 98 film-coated tablets.
PVC/PVDC/Aluminium transparent perforated unit dose blisters with 10 x 1 film-coated tablets. Pack size of 100 × 1 film-coated tablets.
White opaque HDPE bottle with white opaque polypropylene child-resistant screw cap with sealing insert. Pack size of 100 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

Bayer AG
51368 Leverkusen
Germany

8. MARKETING AUTHORISATION NUMBER(S)

Kerendia 10 mg film-coated tablets

EU/1/21/1616/001-005

Kerendia 20 mg film-coated tablets

EU/1/21/1616/006-010

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 February 2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the European Medicines Agency web site: http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

Bayer AG
Kaiser-Wilhelm-Allee
51368 Leverkusen
Germany

Bayer HealthCare Manufacturing S.r.l.
Via delle Groane, 126
20024 Garbagnate Milanese
Italy

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON for 10 mg (blisters and bottle)

1. NAME OF THE MEDICINAL PRODUCT

Kerendia 10 mg film-coated tablets
finerenone

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 10 mg finerenone.

3. LIST OF EXCIPIENTS

Contains lactose. Read the package leaflet before use.

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablet

14 film-coated tablets
28 film-coated tablets
98 film-coated tablets
100 × 1 film-coated tablets
100 film-coated tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Bayer AG
51368 Leverkusen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1616/001 - 14 tablets (blister)
EU/1/21/1616/002 - 28 tablets (blister)
EU/1/21/1616/003 - 98 tablets (blister)
EU/1/21/1616/004 - 100 x 1 tablets (perforated unit dose blister)
EU/1/21/1616/005 - 100 tablets (bottle)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Kerendia 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL for 10 mg

1. NAME OF THE MEDICINAL PRODUCT

Kerendia 10 mg film-coated tablets
finerenone

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 10 mg finerenone.

3. LIST OF EXCIPIENTS

Contains lactose. Read the package leaflet before use.

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablet
100 tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Bayer AG
51368 Leverkusen
Germany

12. MARKETING AUTHORISATION NUMBER

EU/1/21/1616/005 - 100 tablets (bottle)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER for 10 mg

1. NAME OF THE MEDICINAL PRODUCT

Kerendia 10 mg tablets
finerenone

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Bayer AG *(Bayer Logo)*

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Mon. Tue. Wed. Thu. Fri. Sat. Sun.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

UNIT-DOSE BLISTER for 10 mg

1. NAME OF THE MEDICINAL PRODUCT

Kerendia 10 mg tablets
finerenone

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Bayer AG *(Bayer Logo)*

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON for 20 mg (blisters and bottle)

1. NAME OF THE MEDICINAL PRODUCT

Kerendia 20 mg film-coated tablets
finerenone

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 20 mg finerenone.

3. LIST OF EXCIPIENTS

Contains lactose. Read the package leaflet before use.

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablet

14 film-coated tablets
28 film-coated tablets
98 film-coated tablets
100 × 1 film-coated tablets
100 film-coated tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Bayer AG
51368 Leverkusen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1616/006 - 14 tablets (blister)
EU/1/21/1616/007 - 28 tablets (blister)
EU/1/21/1616/008 - 98 tablets (blister)
EU/1/21/1616/009 - 100 x 1 tablets (perforated unit dose blister)
EU/1/21/1616/010 - 100 tablets (bottle)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Kerendia 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL for 20 mg

1. NAME OF THE MEDICINAL PRODUCT

Kerendia 20 mg film-coated tablets
finerenone

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 20 mg finerenone.

3. LIST OF EXCIPIENTS

Contains lactose. Read the package leaflet before use.

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablet
100 tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Bayer AG
51368 Leverkusen
Germany

12. MARKETING AUTHORISATION NUMBER

EU/1/21/1616/010 - 100 tablets (bottle)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER for 20 mg

1. NAME OF THE MEDICINAL PRODUCT

Kerendia 20 mg tablets
finerenone

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Bayer AG *(Bayer Logo)*

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Mon. Tue. Wed. Thu. Fri. Sat. Sun.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

UNIT-DOSE BLISTER for 20 mg

1. NAME OF THE MEDICINAL PRODUCT

Kerendia 20 mg tablets
finerenone

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Bayer AG *(Bayer Logo)*

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Kerendia 10 mg film-coated tablets
Kerendia 20 mg film-coated tablets
finerenone

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Kerendia is and what it is used for
2. What you need to know before you take Kerendia
3. How to take Kerendia
4. Possible side effects
5. How to store Kerendia
6. Contents of the pack and other information

1. What Kerendia is and what it is used for

Kerendia contains the active substance finerenone. Finerenone works by blocking the action of certain hormones (mineralocorticoids) that can damage your kidneys and heart.

Kerendia is used for the **treatment of adults with chronic kidney disease** (with abnormal presence of the protein albumin in the urine) associated with type 2 diabetes.
Chronic kidney disease is a long-term condition. Your kidneys keep getting worse at removing waste and fluids from your blood.
Type 2 diabetes is when your body cannot keep your blood sugar levels normal. Your body does not produce enough of the hormone insulin or cannot use the insulin properly. This leads to a high level of sugar in your blood.

2. What you need to know before you take Kerendia

Do not take Kerendia if you
- are **allergic** to finerenone or any of the other ingredients of this medicine (listed in section 6).
- are taking medicines that belong to the group of 'strong CYP3A4 inhibitors', for example
  - **itraconazole** or **ketoconazole** (to treat fungal infections)
  - **ritonavir**, **nelfinavir**, or **cobicistat** (to treat HIV infection)
  - **clarithromycin**, **telithromycin** (to treat bacterial infections)
  - **nefazodone** (to treat depression).
- have **Addison's disease** (when your body does not produce enough of the hormones 'cortisol' and 'aldosterone').

Warnings and precautions
Talk to your doctor or pharmacist before taking Kerendia if you have
- ever been told you had a high level of potassium in your blood.
- severe loss of kidney function or kidney failure.
- moderate or severe liver problems.
- mild, moderate or severe heart failure. This is when your heart does not pump blood as well as it should. It does not pump enough blood out of the heart in one beat.

Blood tests
These tests **check your potassium level** and **how your kidneys are working**.
Using the results of your blood tests, your doctor decides whether you can start to take Kerendia.
After 4 weeks of taking Kerendia, you will have more blood tests.
Your doctor may test your blood at other times, for example while you are taking certain medicines.

Children and adolescents
Do not give this medicine to children and adolescents under 18 years because it is not known yet whether it is safe and effective in this age group.

Other medicines and Kerendia
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Your doctor will tell you which medicines you can take. Your doctor may need to test your blood to make sure.

You must not take medicines that belong to the group of 'strong CYP3A4 inhibitors,' while taking Kerendia (see section 2 "Do not take Kerendia…").

Talk to your doctor or pharmacist **if you are taking** other medicines while taking Kerendia, especially
- if you take for example
  - **amiloride** or **triamterene** (to remove excess water from your body in the urine)
  - **eplerenone, esaxerenone, spironolactone,** or **canrenone** (medicines similar to finerenone)
  - **trimethoprim**, or a **combination of trimethoprim and sulfamethoxazole** (to treat bacterial infections)
  - **potassium supplements**, including some salt substitutes

  or if you take other medicines that may increase the level of potassium in your blood. These medicines may be unsafe for you.

- if you take for example
  - **erythromycin** (to treat bacterial infections)
  - **verapamil** (to treat high blood pressure, chest pain, and fast heartbeat)
  - **fluvoxamine** (to treat depression and 'obsessive-compulsive disorder')
  - **rifampicin** (to treat bacterial infections)
  - **carbamazepine**, **phenytoin**, or **phenobarbital** (to treat epilepsy)
  - **St. John´s Wort** (*Hypericum perforatum*) (a herbal medicine to treat depression)
  - **efavirenz** (to treat HIV infection)

  or if you take other medicines that belong to the same groups of medicines as the ones listed above (certain 'CYP3A4 inhibitors' and 'inducers'). You may have more side effects, or Kerendia may not work as expected.

- if you take several other **blood pressure lowering medicines**. Your doctor may need to watch your blood pressure.

Kerendia with food and drink
Do not eat grapefruit or drink grapefruit juice as long as you take Kerendia.
If you do, you may get too much finerenone in your blood. **You may have more side effects** (possible side effects are listed in section 4).

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy
You should **not take** this medicine during pregnancy **unless** your doctor states it is clearly necessary. There might be a risk to your unborn baby. Your doctor will discuss that with you.
You should **use reliable birth control** if you are able to become pregnant. Your doctor will explain to you what type of birth control you can use.

Breast-feeding
You should **not breast-feed** while taking this medicine. It may harm your baby.

Driving and using machines
Kerendia has no effect on your ability to drive or use machines.

Kerendia contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

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

3. How to take Kerendia

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much you have to take
The recommended and the **maximum daily dose** of this medicine is **1 tablet** of **20 mg**.

- Always take **1 tablet once daily**. Each tablet contains 10 mg or 20 mg finerenone.
- The **starting dose** depends on how well your kidneys work. To check this your doctor will test your blood. The results help your doctor to decide, if you can start with **1 tablet** of **20 mg or 10 mg** once daily.
- **After 4 weeks** your doctor will test your blood again. Your doctor will decide on the correct dose for you. This might be **1 tablet** of **20 mg or 10 mg** once daily.
  Your doctor may also tell you to interrupt or stop taking Kerendia.

Your doctor may decide on **changes in your treatment** after **testing your blood**. See "Blood tests" in section 2 for more information.

How to take this medicine
Kerendia is taken by mouth. Take Kerendia at the same time every day. This makes it easier for you to remember.

Swallow the tablet whole.
- You can take it with a glass of water.
- You can take it with or without food.
- Do not take it with grapefruit juice or grapefruit. See "Kerendia with food and drink" in section 2 for more information.

If you cannot swallow the tablet whole, you can crush it.
- Mix it with water or soft foods, such as apple sauce.

- Take it right away.

If you take more Kerendia than you should
Talk to your doctor or pharmacist if you think you have taken too much of this medicine.

If you forget to take Kerendia
If you forget to take your tablet at **your regular time that day**
►take the tablet as soon as you notice it that day.

If you **miss a day**
►take the next tablet on the next day, at your regular time.

Do not take 2 tablets to make up for a forgotten tablet.

If you stop taking Kerendia
Only stop taking Kerendia if your doctor has told you.
Your doctor may decide this after testing your blood.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Side effects that your doctor may see in your blood test results
very common (may affect more than 1 in 10 people)
- high potassium level (hyperkalaemia)
  Possible signs of high potassium level in the blood may include weakness or tiredness, feeling sick (nausea), numbness in the hands and lips, muscle cramps, decreased pulse rate.

common (may affect up to 1 in 10 people)
- low sodium level (hyponatraemia)
  Possible signs of low sodium level in the blood may include feeling sick (nausea), tiredness, headache, confusion; muscle weakness, spasms or cramps.
- decrease in how well the kidneys filter blood (glomerular filtration rate decreased).
- high uric acid level (hyperuricaemia)

uncommon (may affect up to 1 in 100 people)
- decrease in a protein (haemoglobin) that is found in your red blood cells.

Other side effects
common (may affect up to 1 in 10 people)
- low blood pressure (hypotension)
  Possible signs of low blood pressure may include dizziness, lightheadedness, fainting.
- itching (pruritus)

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Kerendia

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the blister, bottle label and carton after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Kerendia contains
- The active substance is finerenone.
  - Each tablet of Kerendia **10 mg film-coated tablets** contains 10 mg finerenone.
  - Each tablet of Kerendia **20 mg film-coated tablets** contains 20 mg finerenone.
- The other ingredients are:
  - Tablet core: microcrystalline cellulose, croscarmellose sodium, hypromellose 2910, lactose monohydrate, magnesium stearate, sodium laurilsulfate. See "Kerendia contains lactose" and "Kerendia contains sodium" in section 2 for more information.
  - Tablet coat: hypromellose 2910, titanium dioxide, talc, iron oxide red (E 172, in Kerendia **10 mg film-coated tablets** only), iron oxide yellow (E 172, in Kerendia **20 mg film-coated tablets** only).

What Kerendia looks like and contents of the pack
Kerendia **10 mg film-coated tablets** (tablets) are pink and oval-oblong, 10 mm long and 5 mm wide, marked '10' on one side and 'FI' on the other side.

Kerendia **20 mg film-coated tablets** (tablets) are yellow and oval-oblong, 10 mm long and a 5 mm wide, marked '20' on one side and 'FI' on the other side.

Kerendia is available in cartons containing
- 14, 28 or 98 film-coated tablets.
  Each calendarised transparent blister contains 14 film-coated tablets.

- 100 × 1 film-coated tablets.
  Each perforated transparent unit dose blister contains 10 film-coated tablets.

- 100 film-coated tablets in a plastic bottle.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Bayer AG
51368 Leverkusen
Germany

Manufacturer

You can find out who made Kerendia by looking at what is printed after ‘Lot’ on the carton, blisters or bottle label.

If the batch number starts with ‘BX’, it is:
Bayer AG
Kaiser-Wilhelm-Allee
51368 Leverkusen
Germany

If the batch number starts with ‘IT’, it is:
Bayer HealthCare Manufacturing S.r.l.
Via delle Groane, 126
20024 Garbagnate Milanese
Italy

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.