swissmedic

Date: 27 January 2026
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report
Extension of therapeutic indication

Kerendia

International non-proprietary name:	finerenone
Pharmaceutical form:	film-coated tablets
Dosage strength(s):	10 mg, 20 mg, new: 40 mg
Route(s) of administration:	oral
Marketing authorisation holder:	Bayer (Schweiz) AG
Marketing authorisation no.:	68130
Decision and decision date:	approved on 9 January 2026

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, Definitions, Abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
eGFR	Estimated glomerular filtration rate
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
LVEF	Left ventricular ejection fraction
MAH	Marketing authorisation holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
RMP	Risk management plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

Extension(s) of the therapeutic indication(s)
The applicant requested the addition of a new therapeutic indication or modification of an approved one in accordance with Article 23 TPO.

Work-sharing procedure
The applicant requested a work-sharing procedure with Australia and Canada.
The Access NAS (new active substance) work-sharing initiative is a collaboration between regulatory authorities – specifically Australia's Therapeutic Goods Administration (TGA), Health Canada (HC), Singapore's Health Sciences Authority (HSA), the UK Medicines & Healthcare products Regulatory Agency (MHRA), and Swissmedic – and the pharmaceutical industry.
The work-sharing initiative involves the coordinated assessment of NAS applications and their extensions that have been filed in at least 2 jurisdictions.

2.2 Indication and dosage

2.2.1 Requested indication

Heart failure
Kerendia is indicated for the treatment of chronic symptomatic heart failure with a left ventricular ejection fraction (LVEF) ≥40% in adult patients (see sections "Dosage/Administration" and "Clinical efficacy").

2.2.2 Approved indication

Heart failure
Kerendia is indicated for the treatment of chronic symptomatic heart failure in adult patients with a left ventricular ejection fraction (LVEF) ≥ 40% (see sections "Dosage/Administration" and "Clinical Efficacy").

2.2.3 Requested dosage

Summary of the requested standard dosage:

Usual dosage
Heart failure
In patients with heart failure (LVEF ≥40%), initiation of Kerendia treatment is recommended when serum potassium is ≤5.0 mmol/L. For monitoring of serum potassium, see "Maintenance therapy".

Starting dose for all indications
To determine the starting dose, the estimated glomerular filtration rate (eGFR) is measured. The starting dose of Kerendia is:
• 20 mg once daily if eGFR is ≥ 60 mL/min/1.73 m^2
• 10 mg once daily if eGFR is ≥ 25 to < 60 mL/min/1.73 m^2

Initiation of treatment with Kerendia is not recommended in patients with eGFR < 25 mL/min/1.73 m^2 due to limited clinical experience.

Maintenance therapy
Four weeks after initiation, re-start or dose adjustment of treatment with Kerendia, serum potassium and eGFR must be measured again. See Table 2 to determine continuation of treatment with Kerendia and dose adjustment. Thereafter, serum potassium should be measured periodically and measurement should be repeated as needed based on patient characteristics and serum potassium level.

Table 2: Continuation (4 weeks after initiation or re-start) of treatment and dose adjustment in patients with heart failure

Serum potassium (mmol/L)	**Kerendia dosage (from week 5)**
< 5.0	At a dosage of 10 mg once daily, increase the dosage to 20 mg once daily.* At a dosage of 20 mg once daily, either maintain the dosage or when eGFR ≥60 mL/min/1.73m^2 at treatment initiation, increase the dosage to 40 mg once daily.* Maintain target dose of 40 mg once daily.
5.0 to < 5.5	Maintain dosage.
5.5 to < 6.0	Decrease to next lower dose. Withhold Kerendia if on 10 mg once daily. Restart at 10 mg once daily when serum potassium is <5.5 mmol/L.
≥ 6.0	Withhold Kerendia. Restart at 10 mg once daily when serum potassium is <5.5 mmol/L.**
* If eGFR has not decreased by >30% compared to prior measurement. ** If repeated measurements are ≥5.5 mmol/L, restart treatment at 10 mg once daily when <5.0 mmol/L.	

Special dosage instructions
Patients with hepatic disorders
Severe hepatic impairment (Child-Pugh C): treatment with Kerendia must be avoided

Mild to moderate hepatic impairment (Child-Pugh A or B): no initial dose adjustment is required
In patients with moderate hepatic impairment (Child-Pugh B), additional monitoring of serum potassium should be considered and monitoring should be adapted according to patient characteristics.

Patients with renal disorders
Initiation of treatment
eGFR ≥ 25 to < 60 mL/min/1.73 m^2: the starting dose is 10 mg once daily.
eGFR < 25 mL/min/1.73 m^2: initiation of treatment with Kerendia is not recommended due to limited clinical experience.

Maintenance therapy
Mild, moderate, or severe renal impairment: continued treatment with Kerendia and dose adjustment should proceed based on serum potassium.
To determine whether the starting dose can be increased to the recommended daily dose, the eGFR should be determined 4 weeks after initiation of treatment.

End-stage renal failure (eGFR < 15 mL/min/1.73 m^2): treatment with Kerendia should be continued cautiously with regard to the serum potassium level, as clinical experience is limited

Combination therapy
In all patients already being treated with a moderate CYP3A4 inhibitor, therapy with Kerendia should be initiated at a starting dose of 10 mg once daily.

Body weight: No dose adjustment based on body weight is required.

Elderly patients: No dose adjustment based on age is required.

Children and adolescents: Safety and efficacy in patients under 18 years have not been investigated.

Delayed administration
A missed dose should be taken as soon as possible, but only on the same day. No double dose should be taken on the same day to make up for a missed dose.

Mode of administration
For oral intake with a glass of water independently of meals.
Tablets can be crushed immediately prior to use and taken with water or semi-solid foods (such as apple puree).
Grapefruit or grapefruit juice must be avoided.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	24 February 2025
Formal control completed	26 March 2025
List of Questions (LoQ)	24 July 2025
Response to LoQ	22 September 2025
Preliminary decision	6 November 2025
Response to preliminary decision	21 November 2025
Final decision	9 January 2026
Decision	approval

3 Quality aspects

Swissmedic has not assessed the primary data relating to quality aspects submitted with this application and relies on the assessment of the foreign reference authority, Australia's Therapeutic Goods Administration (see section 2.1 Applicant's request / Work-sharing procedure).

4 Nonclinical aspects

4.1 Nonclinical conclusions

To support the approval of the new 40 mg dosage strength of Kerendia in the requested new indication, the applicant submitted new *in vitro* studies investigating Kerendia's inhibitory potential towards transporters. No additional concern was identified. In addition, a new 13-week juvenile toxicity study in rats was submitted to support the paediatric development programme. Since the paediatric population is not included in the current application, this study was not considered relevant for evaluation of the requested new dosage strength and intended indication extension. No additional nonclinical studies were submitted. This was considered acceptable since there are no nonclinical concerns identified regarding posology and method of administration. Environmental risk assessment studies have shown that Kerendia may pose a risk for surface water and groundwater.

From the nonclinical point of view, there are no objections to approval of the proposed extension of indication and new dosage strength.

5 Clinical aspects

Swissmedic has not assessed the primary data relating to clinical aspects submitted with this application and relies on the assessment of the foreign reference authority, Health Canada (see section 2.1 Applicant’s request / Work-sharing procedure).

6 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

7 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Kerendia was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

Kerendia®

Composition

Active substances

Finerenone.

Excipients

Microcrystalline cellulose, croscarmellose sodium, lactose monohydrate, magnesium stearate, hypromellose, sodium lauryl sulfate.
Film coating: Hypromellose, talc, titanium dioxide (E 171), ferric oxide red (E 172) (contained only in the 10 mg and 40 mg dose strengths), ferric oxide yellow (E 172) (contained only in the 20 mg and 40 mg dose strengths).
One 10 mg film-coated tablet contains 0.44 mg sodium and 42.75 mg lactose.
One 20 mg film-coated tablet contains 0.47 mg sodium and 38.00 mg lactose.
One 40 mg film-coated tablet contains 1.49 mg sodium and 23.75 mg lactose.

Pharmaceutical form and active substance quantity per unit

Film-coated tablets containing 10 mg, 20 mg and 40 mg finerenone.

Appearance

10 mg: pink, oval 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.
20 mg: pale yellow, oval 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.
40 mg: grey-orange, oval film-coated tablet with a length of 11 mm and a width of 5 mm, marked “40” on one side and “FI” on the other side.

Indications/Uses

Chronic kidney disease

Kerendia is indicated to delay progression of chronic kidney disease in adult patients with type 2 diabetes mellitus (see sections “Dosage/Administration” and “Clinical efficacy”).
For study outcomes regarding the effects on cardiovascular events, see section “Clinical efficacy”.

Heart failure

Kerendia is indicated for the treatment of chronic symptomatic heart failure in adult patients with a left ventricular ejection fraction (LVEF) ≥ 40% (see sections “Dosage/Administration” and “Clinical Efficacy”).

Dosage/Administration

Usual dosage

Chronic kidney disease

The recommended target dose of Kerendia is 20 mg once daily (equivalent to the maximum daily dose).

Heart failure

The recommended target dose of Kerendia depends on renal function (eGFR) at initiation of Kerendia treatment (see Table 2):

- 40 mg once daily if eGFR ≥ 60 mL/min/1.73 m^2 (equivalent to the maximum daily dose)
- 20 mg once daily if eGFR ≥ 25 to < 60 mL/min/1.73 m^2

Initiation of treatment

Chronic kidney disease

Kerendia should be used in addition to standard of care (see section “Clinical efficacy”).
In patients with chronic kidney disease with type 2 diabetes, initiation of treatment with Kerendia is recommended when the serum potassium level is ≤4.8 mmol/L.
If the serum potassium level is > 4.8 to 5.0 mmol/L, initiation of treatment with Kerendia can be considered depending on patient characteristics and the serum potassium level, with additional monitoring of serum potassium performed in the first 4 weeks (see section “Warnings and precautions”).
If the serum potassium level is > 5.0 mmol/L, treatment with Kerendia is not recommended (see section “Warnings and precautions”).

Heart failure

Kerendia treatment in patients with heart failure (LVEF ≥ 40%) should only be initiated if the serum potassium level is ≤ 5.0 mmol/L (see section “Warnings and precautions”).

For monitoring of serum potassium, see “Maintenance therapy”.

Starting dose for all indications

To determine the starting dose, the estimated glomerular filtration rate (eGFR) is measured. The starting dose of Kerendia is:

- 20 mg once daily if eGFR ≥ 60 mL/min/1.73 m^2
- 10 mg once daily if eGFR ≥ 25 to < 60 mL/min/1.73 m^2

Initiation of treatment with Kerendia is not recommended in patients with eGFR < 25 mL/min/1.73 m^2 due to limited clinical experience.

Maintenance therapy

Four weeks after initiation, re-start or dose adjustment of treatment with Kerendia, serum potassium and eGFR must be measured again. See Table 1 or 2 to determine continuation of treatment with Kerendia and dose adjustment. Thereafter, serum potassium should be measured periodically and measurement should be repeated as needed based on patient characteristics and serum potassium level (see sections “Warnings and precautions” and “Interactions”).

Chronic kidney disease

Table 1: Continuation (4 weeks after initiation or re-start) of treatment with Kerendia and dose adjustment in patients with chronic kidney disease

Serum potassium (mmol/L)	*Kerendia dosage (from week 5)*
≤ 4.8	Maintain a dosage of 20 mg once daily. At a dosage of 10 mg once daily, increase the dosage to 20 mg once daily if eGFR has not decreased by > 30% compared to the previous measurement.
> 4.8–5.5	Maintain dosage.
> 5.5	Withhold Kerendia. Restart at 10 mg once daily when serum potassium is ≤ 5.0 mmol/L.

Heart failure

Table 2: Continuation (4 weeks after initiation or re-start) of treatment with Kerendia and dose adjustment in patients with heart failure

Serum potassium (mmol/L)	*Kerendia dosage (from week 5)*
< 5.0	At a dosage of 10 mg once daily, increase dosage to 20 mg once daily.* At a dosage of 20 mg once daily, either maintain the dosage, or if eGFR ≥ 60 mL/min/1.73 m^2 at initiation of treatment, increase dosage to 40 mg once daily.* Maintain target dosage of 40 mg once daily.
5.0 to < 5.5	Maintain dosage.

5.5 to < 6.0	Decrease to next lower dose. Withhold Kerendia if on 10 mg once daily. Restart at 10 mg once daily when serum potassium is <5.5 mmol/L.
≥ 6.0	Withhold Kerendia. Restart at 10 mg once daily when serum potassium is <5.5 mmol/L.**
*If eGFR has not decreased by > 30% compared to the previous measurement. **If repeated measurements ≥ 5.5 mmol/L, restart treatment at 10 mg once daily when < 5.0 mmol/L.	

Special dosage instructions

Patients with hepatic disorders

In patients with severe hepatic impairment (Child-Pugh C), treatment with Kerendia must be avoided (see sections “Warnings and precautions” and “Pharmacokinetics”).
In patients with mild to moderate hepatic impairment, no initial dose adjustment is required (Child-Pugh A or B) (see section “Pharmacokinetics”).
In patients with moderate hepatic impairment (Child-Pugh B), additional monitoring of serum potassium should be considered, and monitoring should be adapted based on patient characteristics (see sections “Warnings and precautions” and “Pharmacokinetics”).

Patients with renal disorders

Initiation of treatment

In patients with eGFR ≥ 25 to < 60 mL/min/1.73 m^2, the starting dose of Kerendia is 10 mg once daily.
In patients with eGFR < 25 mL/min/1.73 m^2, initiation of treatment with Kerendia is not recommended due to limited clinical experience (see sections “Warnings and precautions” and “Pharmacokinetics”).

Maintenance therapy

In patients with mild, moderate or severe renal impairment, continued treatment with Kerendia and dose adjustment should proceed based on serum potassium.
To determine whether the starting dose can be increased to the recommended daily dose, the eGFR should be determined 4 weeks after initiation of treatment. See Table 1 or 2 and “Maintenance treatment”.
In patients with end-stage renal failure (eGFR < 15 mL/min/1.73 m^2), treatment with Kerendia should be continued cautiously with regard to the serum potassium level, as clinical experience is limited (see section “Warnings and precautions”).

Combination therapy

In all patients already being treated with a moderate CYP3A4 inhibitor, therapy with Kerendia should be initiated at a starting dose of 10 mg once daily (see sections “Warnings and precautions” and “Interactions”).

Body weight

No dose adjustment based on body weight is required (see section “Pharmacokinetics”).

Elderly patients

No dose adjustment based on age is required (see section “Pharmacokinetics”).

Paediatric population

The safety and efficacy of Kerendia in patients under 18 years have not been investigated.

Delayed administration

A missed dose should be taken as soon as possible, but only on the same day. No double dose should be taken on the same day to make up for a missed dose.

Method of administration

For oral use.
The tablets can be taken with a glass of water independently of meals (see section “Pharmacokinetics”).
Taking Kerendia together with grapefruit or grapefruit juice must be avoided (see sections “Warnings and precautions” and “Interactions”).
For patients unable to swallow whole tablets, the tablets can be crushed immediately prior to use and taken with water or semi-solid foods (such as applesauce) (see section “Pharmacokinetics”).

Contraindications

Kerendia is contraindicated in patients:

- receiving concomitant treatment with strong CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, ritonavir, nelfinavir, cobicistat, clarithromycin, telithromycin and nefazodone) (see section “Interactions”).
- with Addison’s disease.
- with hypersensitivity to the active substance or to any of the excipients (see sections “Composition” and “Warnings and precautions”).

Warnings and precautions

Hyperkalaemia

Hyperkalaemia has been observed in patients treated with Kerendia (see section “Undesirable effects”).

Some patients are at increased risk of developing hyperkalaemia. Risk factors include reduced eGFR, increased serum potassium and previous episodes of hyperkalaemia. More frequent monitoring should be considered in these patients. Local guidelines for the treatment of hyperkalaemia must be observed.
Initiation of treatment with Kerendia is not recommended if the serum potassium level is > 5.0 mmol/L.
The algorithms for dose adjustments in patients with chronic kidney disease or patients with heart failure, as described in section “Dosage/Administration”, must be strictly followed.
In all patients, serum potassium and eGFR must be remeasured four weeks after initiation, re-start or dose adjustment of treatment with Kerendia. Thereafter, serum potassium should be measured periodically and repeated as needed based on patient characteristics and the serum potassium level (see section “Dosage/Administration”).

Concomitant treatment

The risk of hyperkalaemia can also increase in patients taking concomitant medication that can increase the serum potassium level (see section “Interactions”). See also “Concomitant use of substances that influence finerenone exposure”.
Concomitant use of Kerendia with the following medicinal products must be avoided:

- potassium-sparing diuretics (e.g. amiloride, triamterene)
- other mineralocorticoid receptor antagonists (MRAs) (e.g. eplerenone, esaxerenone, spironolactone, canrenone)

Kerendia must be used with caution and the serum potassium level must be monitored when Kerendia is taken concomitantly with the following medicinal products:

- potassium supplements
- trimethoprim or trimethoprim-sulfamethoxazole. Temporary interruption of treatment with Kerendia may be required.

Renal impairment

The risk of hyperkalaemia increases with decreasing renal function. Continuous monitoring of renal function should be performed as needed in accordance with standard practice (see section “Dosage/Administration”).
Initiation of treatment with Kerendia is not recommended in patients with eGFR < 25 mL/min/1.73 m^2 due to limited clinical experience (see sections “Dosage/Administration” and “Pharmacokinetics”).
In patients with end-stage renal failure (eGFR < 15 mL/min/1.73 m^2), treatment with Kerendia should be continued cautiously with regard to the serum potassium level, as clinical experience is limited (see section “Dosage/Administration”).

Hepatic impairment

Patients with severe hepatic impairment (Child-Pugh C) have not been studied (see section “Pharmacokinetics”). Due to an expected substantial increase in finerenone exposure, the use of

Kerendia in patients with severe hepatic impairment should be avoided (see section “Dosage/Administration”).
Due to an increase in finerenone exposure, additional monitoring of serum potassium should be considered in patients with moderate hepatic impairment (Child-Pugh B) and monitoring should be adapted based on patient characteristics (see sections “Dosage/Administration” and “Pharmacokinetics”).

Concomitant use of substances that influence finerenone exposure

Moderate and weak CYP3A4 inhibitors

When Kerendia is co-administered with moderate CYP3A4 inhibitors (e.g. erythromycin and verapamil) or weak CYP3A4 inhibitors (e.g. amiodarone and fluvoxamine), increased finerenone exposure is expected (see section “Interactions”). The serum potassium level must therefore be monitored particularly during initiation of treatment with – or when changing the dosage of – Kerendia or the CYP3A4 inhibitor (see section “Dosage/Administration”).

Strong and moderate CYP3A4 inducers

Concomitant use of Kerendia with strong CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, St John’s wort) or moderate CYP3A4 inducers (e.g. efavirenz) that markedly decrease the plasma concentrations of finerenone and lead to a reduced therapeutic effect must be avoided (see section “Interactions”). Use of an alternative co-medication with no or weak potential to induce CYP3A4 should be considered.

Grapefruit

Concomitant ingestion of grapefruit or grapefruit juice must be avoided, as this increases the plasma concentration of finerenone (see sections “Dosage/Administration” and “Interactions”).

Embryofetal toxicity

Kerendia must not be used during pregnancy unless there has been careful consideration of the benefit for the mother and the risk to the fetus. If a woman becomes pregnant while taking Kerendia, she must be informed of the potential risks to the unborn child. Women of childbearing potential should be advised to use an effective method of contraception during treatment with Kerendia. Women should be advised not to breast-feed during treatment with Kerendia. For further information, see sections “Pregnancy, lactation” and “Preclinical data”.

Information on excipients

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

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

Interactions

Interaction studies have only been performed in adults. Finerenone is eliminated almost exclusively via cytochrome P450 (CYP)-mediated oxidative metabolism (mainly via CYP3A4 [90%] and, to a minor extent, via CYP2C8 [10%]).

Effect of other medicinal products on Kerendia

Enzyme inhibitors

Strong CYP3A4 inhibitors

Concomitant use of Kerendia with itraconazole, clarithromycin and other strong CYP3A4 inhibitors (e.g. ketoconazole, ritonavir, nelfinavir (not approved in Switzerland), cobicistat, telithromycin (not approved in Switzerland) or nefazodone (not approved in Switzerland) is contraindicated, as a significant increase in finerenone exposure can be expected (see section “Contraindications”). Simulations show that concomitant use of Kerendia with itraconazole (200 mg twice daily) increases finerenone exposure (geometric mean ratio (GMR) and 90% population interval for AUC and C_{max}: 6.31 [3.36-11.41] and 2.37 [1.76-3.31]). Clarithromycin (500 mg twice daily) also leads to an anticipated increase in finerenone exposure (GMR and 90% population interval for AUC and C_{max}: 5.28 [2.88-10.48] and 2.25 [1.76-2.98]).

Moderate CYP3A4 inhibitors

Concomitant use of erythromycin (500 mg thrice daily), a moderate CYP3A4 inhibitor, increased mean finerenone exposure (GMR and 90% confidence interval for AUC and C_{max}: 3.48 [3.02-4.02] and 1.88 [1.63-2.17]). Another moderate CYP3A4 inhibitor, verapamil (240 mg sustained-release tablet once daily), increased mean finerenone exposition (GMR and 90% confidence interval for AUC and C_{max}: 2.70 [2.43-3.01] and 2.22 [1.88-2.62]). Since serum potassium can therefore rise, the serum potassium level must be monitored (see sections “Dosage/Administration” and “Warnings and precautions”).

Weak CYP3A4 inhibitors

Simulations indicate that fluvoxamine (100 mg twice daily), a weak CYP3A4 inhibitor, increases finerenone exposure (GMR and 90% population interval for AUC and C_{max}: 1.57 [1.25-2.08] and 1.38 [1.18-1.64]). Since serum potassium can therefore rise, the serum potassium level must be monitored (see sections “Dosage/Administration” and “Warnings and precautions”).

Grapefruit

Concomitant intake of grapefruit or grapefruit juice is likely to increase the plasma concentration of finerenone and should be avoided (see sections “Dosage/Administration” and “Warnings and precautions”).

Enzyme inducers

Concomitant use of Kerendia with rifampicin and other strong CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbital, St John's wort), or with efavirenz and other moderate CYP3A4 inducers is not recommended. These CYP3A4 inducers significantly reduce the plasma concentrations of finerenone and lead to reduced therapeutic effect (see section "Warnings and precautions").
Simulations indicate that rifampicin (600 mg once daily), a strong CYP3A4 inducer, reduces finerenone exposure (GMR and 90% population interval for AUC and C_{max}: 0.07 [0.05-0.11] and 0.14 [0.11-0.21]). Efavirenz (600 mg once daily), a moderate CYP3A4 inducer, reduces finerenone exposure (GMR and 90% population interval for AUC and C_{max}: 0.19 [0.14-0.27] and 0.32 [0.23-0.43]).

Pharmacodynamic interactions

Medicinal products that increase serum potassium

Medicinal products that increase serum potassium can be expected to increase the risk of hyperkalaemia when used concomitantly with Kerendia.
Concomitant use of Kerendia with the following medicinal products should be avoided:

- potassium-sparing diuretics (e.g. amiloride, triamterene (not approved in Switzerland))
- other mineralocorticoid receptor antagonists (MRAs) (e.g. eplerenone, spironolactone, esaxerenone (not approved in Switzerland), canrenone (not approved in Switzerland))

Kerendia should be used with caution when co-administered with the following medicinal products, and the serum potassium level must be monitored during treatment:

- potassium supplements
- trimethoprim or trimethoprim-sulfamethoxazole. Temporary interruption of treatment with Kerendia may be required (see section "Warnings and precautions").

Effect of Kerendia on other medicinal products

CYP3A4 inhibition
At a dose of 40 mg once daily, finerenone is a weak inhibitor of the CYP3A4 enzyme *in vivo*. Co-administration of multiple doses of 40 mg finerenone with the CYP3A4 probe substrate midazolam resulted in a mean increase in the exposure of the CYP3A4 substrate (GMR and 90% confidence interval for AUC and C_{max}: 1.31 [1.23-1.40] and 1.15 [1.08-1.22]). With concomitant use of finerenone 40 mg once daily, the potentially increased exposure of CYP3A4 substrates with a narrow therapeutic window (e.g. tacrolimus, ciclosporin) should be taken into consideration. A multiple-dose regimen of 20 mg finerenone once daily had no effect on the AUC of the CYP3A4 substrate midazolam. At this dosage, finerenone does not elicit inhibition or induction of CYP3A4.

CYP2C8 inhibition

At a dose of 40 mg once daily, finerenone is a weak inhibitor of the CYP2C8 enzyme *in vivo*. Co-administration of multiple doses of 40 mg finerenone with the CYP2C8 reference substrate repaglinide resulted in a mean increase in the exposure of the CYP2C8 substrate (GMR and 90% confidence interval for AUC and C_{max}: 1.59 [1.50-1.69] and 1.30 [1.20-1.41]). With concomitant use of finerenone 40 mg once daily, the potentially increased exposure of CYP2C8 substrates with a narrow therapeutic window (e.g. paclitaxel) should be taken into consideration. A single dose of 20 mg finerenone had no effect on AUC and C_{max} of repaglinide, a CYP2C8 substrate. Finerenone does not inhibit CYP2C8 at this dosage.

Other interactions

No mutual pharmacokinetic interaction was demonstrated between finerenone and the CYP2C9 substrate warfarin. At a dose of 20 mg, finerenone had no clinically relevant effect *in vivo* on the plasma concentration of the P-gp substrate digoxin, which is moreover expected at a dosage of 40 mg. Multiple doses of 40 mg finerenone once daily had no clinically relevant effect on the AUC or C_{max} of of the BCRP and OATP substrate rosuvastatin.

Pregnancy, lactation

Women of childbearing potential

Women who can become pregnant should use effective contraception during treatment with Kerendia.

Pregnancy

There are no data on the use of Kerendia in pregnant women. Animal studies have shown embryofetal developmental toxicity after exposure in excess of the maximum human exposure (see section “Preclinical data”).

Kerendia should not be used during pregnancy, unless treatment with finerenone is required due to the woman’s clinical condition.

Lactation

It is unknown whether finerenone or its metabolites are excreted in human milk. Available pharmacokinetic and toxicological data in animals have shown excretion of finerenone and its metabolites in milk, as well as adverse effects on juvenile animals (see section “Preclinical data”). A risk for breast-fed newborns and infants cannot be excluded. A decision must be made as to whether breastfeeding should be interrupted or whether treatment with Kerendia should be avoided, taking into account both the benefit of breastfeeding for the child and the benefit of therapy for the woman.

Fertility

There are no data on the effect of Kerendia on human fertility. Animal studies with finerenone have revealed no clinically relevant indications of any risk of impaired fertility (see section “Preclinical data”).

Effects on ability to drive and use machines

Based on the safety profile of Kerendia, no influence on the ability to drive or use machines is anticipated.

Undesirable effects

Summary of the safety profile

The safety of Kerendia in patients with chronic kidney disease and type 2 diabetes was evaluated in two randomised, double-blind, placebo-controlled, multicentre phase III studies: in the FIDELIO-DKD and FIGARO-DKD studies, 2818 and 3671 patients, respectively, received Kerendia (10 mg or 20 mg once daily), with a mean duration of treatement of 2.2 and 2.9 years, respectively.
The safety of Kerendia in patients with heart failure (LVEF ≥ 40%) was investigated in FINEARTS-HF, a randomised, double-blind, placebo-controlled, multicentre phase III study. In this study, 2993 patients received Kerendia (10 mg, 20 mg or 40 mg once daily) with a mean duration of treatment of 2.1 years.
The most commonly reported (≥ 10%) adverse reaction with Kerendia was hyperkalaemia (see "Description of selected adverse reactions" below and section "Warnings and precautions").

List of adverse reactions

The adverse reactions observed with Kerendia are summarised in Table 3 below according to MedDRA system organ classes and frequency categories. Adverse reactions are listed by system organ class and in order of declining frequency, using the following convention: Very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10,000, <1/1000) and very rare (<1/10,000).

Table 3: Adverse reactions reported with Kerendia in Phase III studies (pooled data from the FIDELIO-DKD, FIGARO-DKD and FINEARTS-HF studies).

MedDRA System organ class	*Very common*	*Common*
Metabolism and nutrition disorders	Hyperkalaemia[1]	Hyponatraemia[2] Hyperuricaemia[3, 4]
Vascular disorders		Hypotension[5, 6]
Investigations		Blood creatinine increased[7] / Glomerular filtration rate decreased[7]

[1] includes blood potassium increased and hyperkalaemia

[2] includes blood sodium decreased and hyponatraemia

[3] includes blood uric acid increased and hyperuricaemia

[4] Asymptomatic hyperuricemia was observed. In the FIGARO-DKD study, an increase from baseline in mean serum uric acid of up to 0.3 mg/dL was seen in the Kerendia group compared to placebo, which attenuated over time. No hyperuricemia related treatment discontinuations were reported

[5] includes blood pressure decreased, blood pressure diastolic decreased, diastolic hypotension and hypotension

MedDRA System organ class	*Very common*	*Common*
[6] In patients treated with Kerendia, mean systolic blood pressure (SBP) decreased by 3 mmHg and mean diastolic blood pressure (DBP) by 1-2 mmHg after 1 month and remained stable thereafter. The majority of hypotensive events were mild or moderate and resolved spontaneously. Events associated with hypotension, such as dizziness, syncope or fall, were comparable between Kerendia and placebo. [7] An initial small increase in blood creatinine and decrease in glomerular filtration rate (GFR) (mean 2-3 mL/min/1.73 m^2) occurred within the first 4 weeks of starting Kerendia therapy and then stabilized. These changes were reversible after treatment discontinuation.		

Description of selected adverse reactions

Hyperkalaemia

In the FIDELIO-DKD study in patients with chronic kidney disease (mean eGFR 44.4 mL/min/1.73 m^2) and type 2 diabetes, hyperkalaemia events were reported in 18.2% of patients treated with Kerendia, compared with 9.0% of placebo-treated patients. An increase from baseline in the mean serum potassium level of approximately 0.2 mmol/L was observed in the first month of treatment in the Kerendia arm compared with placebo, which remained stable thereafter (see section “Properties/Effects”). The percentage of hospitalisations for hyperkalaemia was 1.4% for the Kerendia group versus 0.3% in the placebo group. The frequency of hyperkalaemia leading to permanent discontinuation of the study product was 2.3% in patients on Kerendia versus 0.9% in the placebo group.
In the FIGARO-DKD study in patients with chronic kidney disease (mean eGFR 67.8 mL/min/1.73 m^2) and type 2 diabetes, hyperkalaemia events were reported in 10.7% of patients treated with Kerendia, compared with 5.3% of placebo-treated patients. An increase from baseline in the mean serum potassium level of approximately 0.15 mmol/L was observed in the first month of treatment in the Kerendia arm compared with placebo, which remained stable thereafter (see section “Properties/Effects”). The percentage of hospitalisations for hyperkalaemia was 0.6% for the Kerendia group versus < 0.1% in the placebo group. The frequency of hyperkalaemia leading to permanent discontinuation of the study product was 1.3% in patients on Kerendia versus 0.4% in the placebo group.

In the FINEARTS-HF study in patients with heart failure (LVEF ≥ 40%), hyperkalaemia events were reported in 9.7% of patients treated with Kerendia compared with 4.2% of placebo-treated patients. An increase from baseline in the mean serum potassium level of approximately 0.2 mmol/L was observed in the first month of treatment in the Kerendia arm compared with placebo, which remained stable thereafter (see section “Properties/Effects”). The percentage of hospitalisations for hyperkalaemia was

0.5% for the Kerendia group versus 0.2% in the placebo group. The frequency of hyperkalaemia leading to permanent discontinuation of the study product was 0.4% in patients on Kerendia versus 0.2% in the placebo group.

In all studies, the majority of hyperkalaemia events were mild to moderate in patients treated with Kerendia. For specific recommendations, see sections “Dosage/Administration” and “Warnings and precautions”.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the EIViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

No cases of adverse events associated with Kerendia overdose in humans have been reported. The most likely sign of an overdose is anticipated to be hyperkalaemia. If hyperkalaemia develops, standard treatment according to local guidelines should be initiated. Treatment with Kerendia should be continued according to Table 1 or 2 (see section “Dosage/Administration”).
Finerenone is unlikely to be efficiently eliminated by haemodialysis, as the fraction bound to plasma proteins is about 90%.

Properties/effects

ATC Code

C03DA05

Mechanism of action

Finerenone is a non-steroidal, selective antagonist of the mineralocorticoid receptor (MR) and effectively attenuates inflammation and fibrosis mediated by MR over-activation. The MR is expressed in the kidneys, heart and blood vessels, where finerenone also counteracts sodium retention and hypertrophic processes. Finerenone has a high potency and selectivity for the MR due to its non-steroidal structure and bulky binding mode. Finerenone has no relevant affinity for androgen, progesterone, oestrogen or glucocorticoid receptors and therefore causes no sex hormone-related adverse reactions (such as gynaecomastia). Its binding to the MR leads to a specific receptor ligand complex that blocks recruitment of transcriptional coactivators implicated in the expression of pro-inflammatory and pro-fibrotic mediators.

Pharmacodynamics

Effects in healthy subjects

Multiple dose regimens (daily doses of 20 mg or 40 mg over 10 days) led to activation of the renin-angiotensin-aldosterone system (RAAS), i.e. reversible increases in plasma renin activity and serum aldosterone concentrations, with baseline values regained within 48 hours after the last dose.
Following activation of the MR with its agonist fludrocortisone, single doses of finerenone up to 20 mg showed dose-dependent natriuretic effects, as well as reduced urinary potassium excretion compared with placebo.
Single or multiple doses of finerenone had no influence on vital signs in healthy subjects.

Effects on urinary albumin-to-creatinine ratio (UACR)

In the two phase III studies FIDELIO-DKD and FIGARO-DKD in patients with chronic kidney disease, the placebo-corrected relative reduction in UACR in patients randomised to treatment with finerenone was 31% and 32% after 4 months, respectively. The reduction in UACR persisted in both studies.
In the phase III FINEARTS-HF study in patients with heart failure (LVEF ≥40%), the placebo-corrected relative reduction in UACR in patients randomized to treatment with finerenone was 30% at 6 months, and UACR remained reduced up to the last measurement at year 2.
In the ARTS-DN study, a randomised, double-blind, placebo-controlled, multicentre phase IIb dose-finding study in adults with chronic kidney disease and type 2 diabetes, 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

An in-depth QT study in 57 healthy subjects produced no indications of a QT/QTc-prolonging effect for finerenone after single doses of 20 mg (therapeutic) or 80 mg (supratherapeutic), suggesting that finerenone has no effect on cardiac repolarisation.

Clinical efficacy

Chronic kidney disease

Finerenone was investigated in two randomised, double-blind, placebo-controlled, multicentre phase III studies: FIDELIO-DKD and FIGARO-DKD.
The FIDELIO-DKD study investigated the effect of finerenone compared to placebo on renal and cardiovascular outcomes in adult patients with type 2 diabetes and chronic kidney disease (inclusion criteria: a) moderate albuminuria [UACR ≥ 30 - < 300 mg/g] and eGFR 25 - 60 mL/min/1.73 m^2 with concomitant presence of diabetic retinopathy OR b) severe albuminuria [UACR ≥ 300 mg/g] and eGFR 25 – 75 mL/min/1.73 m^2). Patients enrolled onto the study were required to have a serum potassium level of ≤ 4.8 mmol/L and to have received previous treatment with standard therapy, including a

maximum tolerated dose of an angiotensin-converting enzyme inhibitor (ACEi [34%]) or an angiotensin-II receptor blocker (ARB [66%]). The indication for treatment with an MRA according to guidelines (such as symptomatic chronic heart failure with reduced ejection fraction) was an exclusion criterion.

The primary endpoint of the FIDELIO-DKD study was a composite of time to first occurrence of kidney failure (defined as chronic dialysis, kidney transplantation or a decrease in eGFR to < 15 mL/min/1.73 m^2 over at least four weeks), a decrease in baseline eGFR by ≥ 40% over at least four weeks or renal death. The key secondary endpoint was a composite cardiovascular endpoint consisting of time to first occurrence of cardiovascular (CV) death, non-fatal myocardial infarction (MI), non-fatal stroke or hospitalisation for heart failure.

The study investigated 5662 patients randomised at a 1:1 ratio to treatment with finerenone once daily (n = 2824) or placebo (n = 2838). The starting dose was either 10 mg [for an eGFR of 25 - < 60 mL/min/1.73 m^2] or 20 mg [for an eGFR of ≥ 60 mL/min/1.73 m^2]. The dose strength was adjusted over the course of the study to 10 mg or 20 mg QD, mainly based on the serum potassium level. Median follow-up was 2.6 years. The study population was 63% white, 25% Asian and 5% black. Mean age at recruitment was 66 years, and 70% of patients were male. Mean baseline eGFR was 44.4 mL/min/1.73 m^2, and 55% of patients had an eGFR of < 45 mL/min/1.73 m^2. Median UACR was 853 mg/g; mean glycated haemoglobin A1c (HbA_{1c}) was 7.7%. About 46% of study participants had a previous atherosclerotic cardiovascular disease, while 30% had a history of coronary heart disease and 8% had a history of heart failure. Mean blood pressure was 138/76 mmHg. The mean duration from diagnosis of type 2 diabetes at study inclusion was 16.6 years and, at study baseline, almost all study participants (97%) were receiving one or more antidiabetic agents (insulin [64%], biguanides [44%], glucagon-like peptide-1 [GLP-1] receptor agonists [7%], sodium-glucose cotransporter 2 [SGLT2] inhibitors [5%]). In addition, 47% and 26% of patients had pre-existing diabetic retinopathy and diabetic neuropathy, respectively, at study baseline. The majority of patients were also receiving a statin (74%) and/or a calcium channel blocker (63%).

The FIDELIO-DKD study demonstrated superiority of treatment with finerenone versus placebo for the combined (renal) primary endpoint (HR 0.82, 95% CI 0.73-0.92, p = 0.0009; see Table 4 and Figure 1). Furthermore, finerenone significantly reduced the risk for the combined (cardiovascular) key secondary endpoint (HR 0.86, 95% CI 0.75–0.99, p = 0.0344; see Table 4 and Figure 2). In the finerenone arm, lower incidence rates were seen compared to the placebo arm with regard to heart failure, non-fatal MI and cardiovascular death. Non-fatal stroke occurred at a similar incidence in both treatment arms (see Table 4).

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

	Patients with chronic kidney disease and type 2 diabetes					
	*Finerenone** *10 or 20 mg once daily* *n = 2824*		*Placebo** *n = 2838*		*Treatment effect Finerenone/Placebo*	
Primary and secondary time-to-event endpoints:	*n (%)*	*Event rate (100 PY.)*	*n (%)*	*Event rate (100 PY.)*	*Hazard Ratio (95% CI)*	*p-value*
Primary combined endpoint “kidney failure, sustained eGFR decrease ≥ 40% or renal death”	498 (17.6%)	7.53	600 (21.1%)	9.09	0.82 [0.73; 0.92]	0.0009
Kidney failure	205 (7.3%)	2.96	235 (8.3%)	3.39	0.86 [0.72; 1.05]	-
Sustained eGFR decrease ≥ 40%	473 (16.7%)	7.15	577 (20.3%)	8.74	0.81 [0.72; 0.91]	-
Renal death	2 (< 0.1%)	-	2 (< 0.1%)	-	-	-
Secondary combined endpoint “CV death, non-fatal MI, non-fatal stroke or hospitalisation for heart failure”	366 (13.0%)	5.11	420 (14.8%)	5.93	0.86 [0.75; 0.99]	0.0344
CV death	128 (4.5%)	1.70	150 (5.3%)	1.99	0.86 [0.68; 1.09]	-
Non-fatal MI	70 (2.5%)	0.94	87 (3.1%)	1.18	0.80 [0.58; 1.09]	-
Non-fatal stroke	90 (3.2%)	1.22	87 (3.1%)	1.18	1.03 [0.77; 1.38]	-
Hospitalisation for heart failure	138 (4.9%)	1.88	162 (5.7%)	2.22	0.85 [0.68; 1.07]	-
* Treatment in addition to maximum tolerated approved doses of ACEi or ARB.						

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

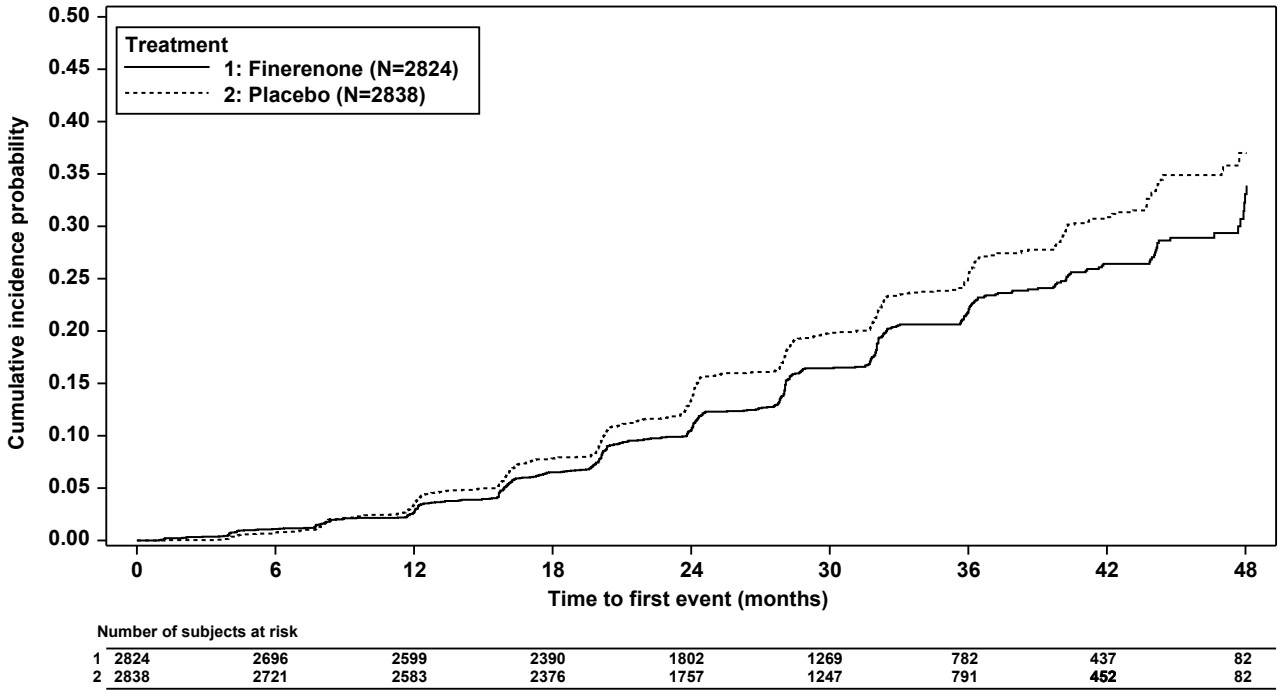
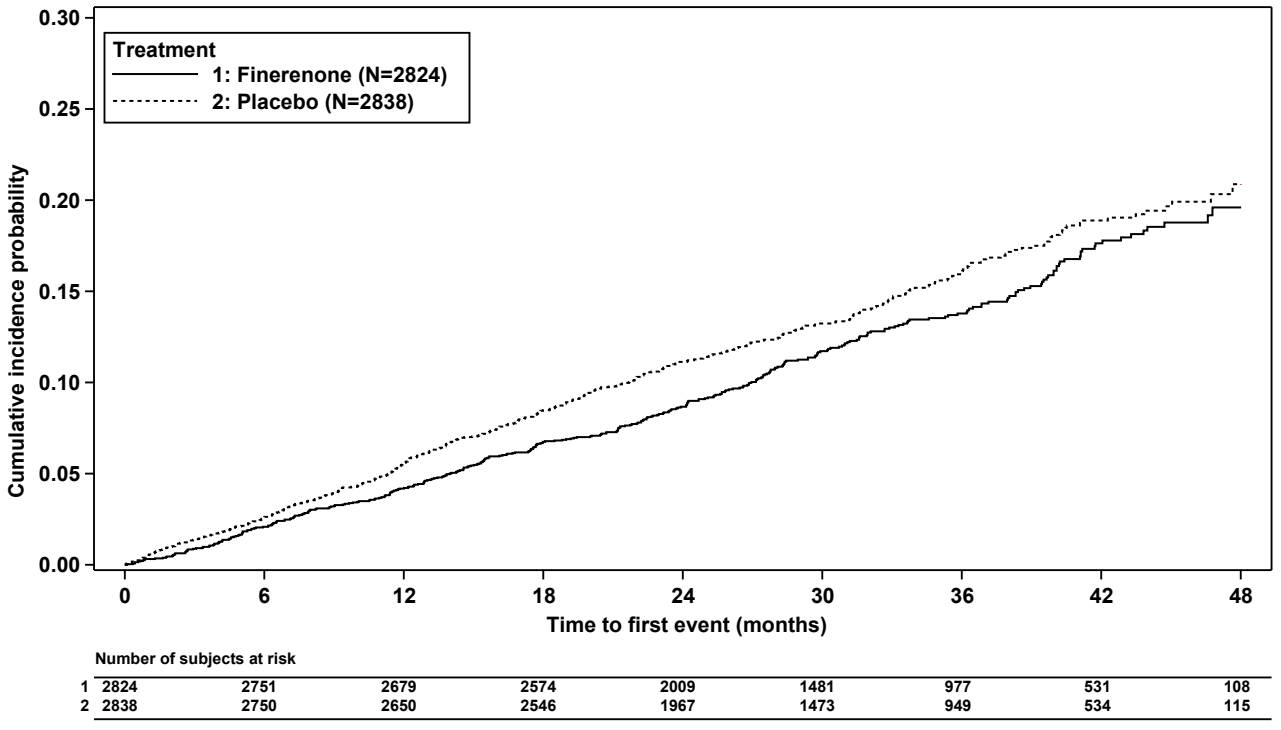


Figure 2: Time to first occurrence of CV death, non-fatal MI, non-fatal stroke or hospitalisation for heart failure in the FIDELIO-DKD study



The FIGARO-DKD study investigated the effect of finerenone compared to placebo on the occurrence of cardiovascular and renal events in adult patients with type 2 diabetes and chronic kidney disease (inclusion criteria: a) moderate albuminuria [UACR ≥ 30 - < 300 mg/g] and eGFR 25 - 90 mL/min/1.73 m^2 OR b) severe albuminuria [UACR ≥ 300 mg/g] and eGFR ≥ 60 mL/min/1.73 m^2). Patients enrolled onto the study were required to have a serum potassium level of ≤ 4.8 mmol/L and to have received previous treatment with standard therapy, including a maximum tolerated dose of an angiotensin-converting enzyme inhibitor (ACEi [43%]) or an angiotensin-II receptor blocker (ARB [57%]). The indication for treatment with an MRA according to guidelines (such as symptomatic chronic heart failure with reduced ejection fraction) was an exclusion criterion.

The primary endpoint in the FIGARO-DKD study was a composite cardiovascular (CV) endpoint consisting of time to first occurrence of CV death, non-fatal MI, non-fatal stroke or hospitalisation for heart failure. The key secondary endpoint was a composite renal endpoint consisting of time to kidney failure, a decrease in baseline eGFR by ≥ 40% over at least four weeks or renal death.

The study investigated 7328 patients randomised at a 1:1 ratio to treatment with finerenone (n = 3674) or placebo (n = 3654). The starting dose was either 10 mg [for an eGFR of 25 - < 60 mL/min/1.73 m^2] or 20 mg [for an eGFR of ≥ 60 mL/min/1.73 m^2]. The dose strength was adjusted over the course of the study to 10 mg or 20 mg QD, mainly based on the serum potassium level. Median follow-up was 3.4 years. The study population was 72% white, 20% Asian and 4% black. Mean age at recruitment was 64 years and 69% of patients were male. Mean baseline eGFR was 67.8 mL/min/1.73 m^2 and 62% of patients had an eGFR of ≥ 60 mL/min/1.73 m^2. Median UACR was 309 mg/g; mean glycated haemoglobin A1c (HbA1c) was 7.7%. About 45% of study participants had a history of atherosclerotic cardiovascular disease, while 8% had a history of heart failure. Mean blood pressure was 136/77 mmHg. The mean duration of type 2 diabetes at study inclusion was 14.5 years and, at study baseline, almost all study participants (98%) were receiving one or more antidiabetic agents (insulin [54%], biguanides [69%], GLP-1 receptor agonists [8%] and SGLT2 inhibitors [8%]). In addition, 31% and 28% of patients had pre-existing diabetic retinopathy and diabetic neuropathy, respectively, at study baseline. The majority of patients were also receiving a statin (71%).

Finerenone significantly reduced the risk for the primary (cardiovascular) combined endpoint compared with placebo (HR 0.87, 95% CI 0.76–0.98, p = 0.0254) (see Figure 3 and Table 5). The treatment effect for the primary endpoint was consistent in all subgroups, including region, eGFR, UACR, systolic blood pressure and HbA1c at baseline. In the finerenone arm, a lower incidence rate of the combined secondary (renal) endpoint of kidney failure, sustained eGFR decrease ≥ 40% or renal death was observed compared to the placebo arm; however, this difference did not reach statistical significance (HR 0.87, 95% CI 0.75–1.01, p = 0.0635) (see Figure 4 and Table 5).

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

	Patients with chronic kidney disease and type 2 diabetes					
	Finerenone 10 or 20 mg once daily n = 3674*		*Placebo* n = 3654*		*Treatment effect Finerenone/Placebo*	
Primary and secondary time-to-event endpoints:	*n (%)*	*Event rate (100 PY.)*	*n (%)*	*Event rate (100 PY.)*	*Hazard Ratio (95% CI)*	*p-value*
Primary combined endpoint “CV death, non-fatal MI, non-fatal stroke or hospitalisation for heart failure”	457 (12.4%)	3.88	518 (14.2%)	4.46	0.87 [0.76; 0.98]	0.0254
CV death	193 (5.3%)	1.56	214 (5.9%)	1.75	0.89 [0.73; 1.08]	-
Non-fatal MI	103 (2.8%)	0.85	101 (2.8%)	0.84	1.00 [0.76; 1.32]	-
Non-fatal stroke	108 (2.9%)	0.89	111 (3.0%)	0.93	0.97 [0.74; 1.26]	-
Hospitalisation for heart failure	117 (3.2%)	0.97	163 (4.5%)	1.36	0.71 [0.56; 0.90]	-
Combined endpoint “kidney failure, sustained eGFR decrease ≥ 40% or renal death”	350 (9.5%)	3.17	395 (10.8%)	3.59	0.87 [0.75; 1.01]	0.0635**
Kidney failure	46 (1.3%)	0.40	62 (1.7%)	0.55	0.72 [0.49; 1.05]	-
Sustained eGFR decrease ≥ 40%	338 (9.2%)	3.06	385 (10.5%)	3.50	0.86 [0.74; <1.00]	-
Renal death	0	-	2 (< 0.1%)	-	-	-

* Treatment in addition to maximum tolerated approved doses of ACEi or ARB.

** Not significant.

Figure 3: Time to first occurrence of CV death, non-fatal MI, non-fatal stroke or hospitalisation for heart failure in the FIGARO-DKD study

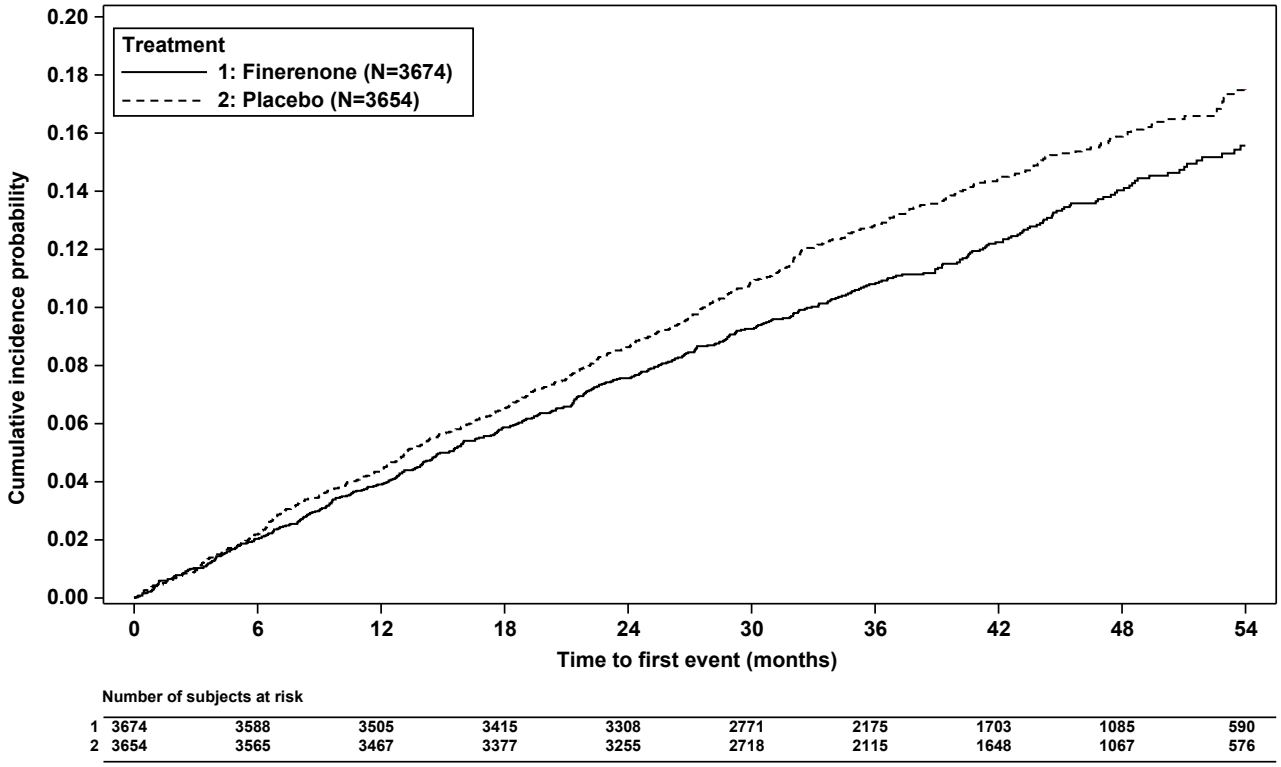
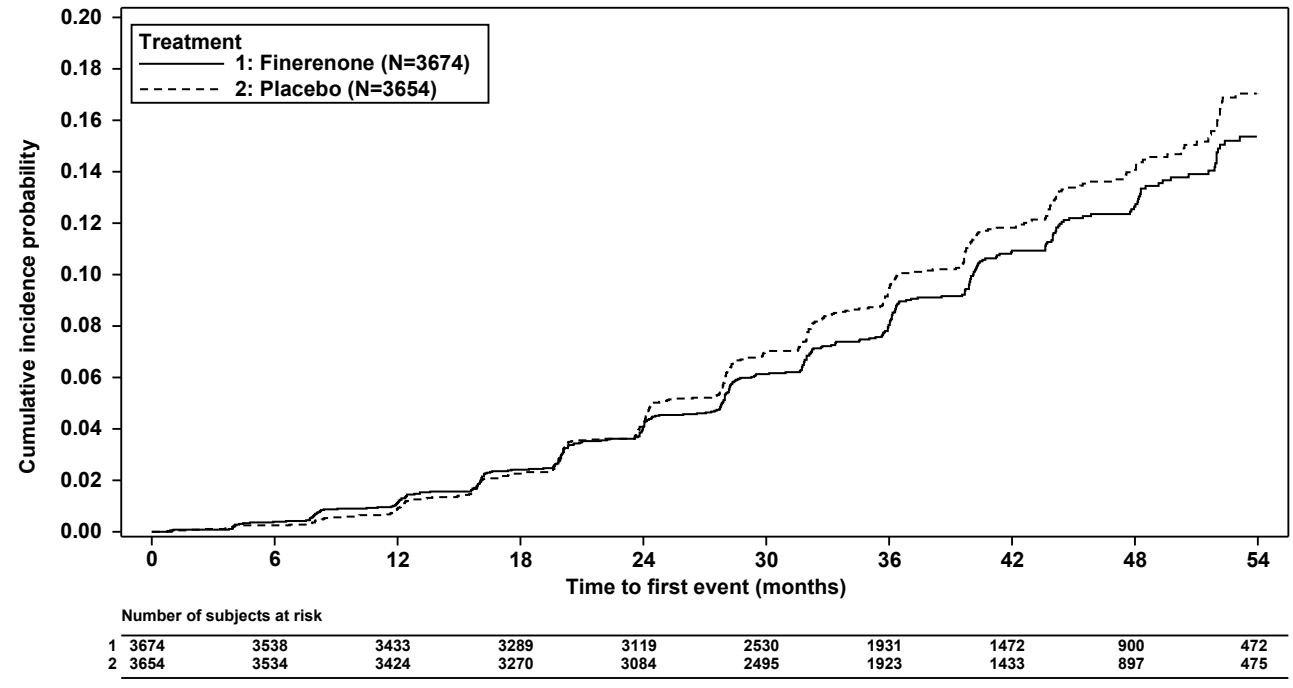


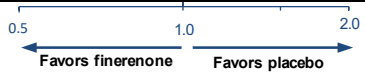
Figure 4: Time to first occurrence of kidney failure, sustained eGFR decrease ≥ 40% versus baseline or renal death in the FIGARO-DKD study



In a pre-specified pooled analysis of the FIDELIO-DKD and FIGARO-DKD studies, finerenone reduced the risk for the combined cardiovascular endpoint “Time to occurrence of CV death, non-fatal MI, non-fatal stroke or hospitalisation for heart failure” compared with placebo (HR 0.86 [95% CI 0.78; 0.95]) (see Figure 5). The risk for the combined renal endpoint “Time to occurrence of kidney failure, sustained eGFR decrease ≥ 40% versus baseline or renal death” was also reduced with finerenone compared with placebo (HR 0.84 [95% CI 0.77; 0.92]), as was the combined endpoint of time to occurrence of kidney failure, sustained eGFR decrease ≥ 57% (corresponding to approximately a doubling of serum creatinine) versus baseline or renal death (HR 0.76 [95% CI 0.66; 0.88]) (see Figure 5).

Figure 5: Combined cardiovascular and renal endpoints in the pooled analysis of FIDELIO-DKD and FIGARO-DKD

Outcome	Finerenone (n=6498)		Placebo (n=6492)		Hazard ratio (95% CI)
	Number of patients with event (%)	Number of patients with event per 100 patient-years	Number of patients with event (%)	Number of patients with event per 100 patient-years	
Composite cardiovascular outcome	823 (12.7)	4.34	938 (14.4)	5.02	0.86 (0.78–0.95)
Death from cardiovascular causes	321 (4.9)	1.61	364 (5.6)	1.84	0.88 (0.75–1.02)
Non-fatal myocardial infarction	173 (2.7)	0.88	188 (2.9)	0.97	0.91 (0.74–1.12)
Non-fatal stroke	198 (3.0)	1.01	198 (3.0)	1.02	0.99 (0.82–1.21)
Hospitalisation for heart failure	255 (3.9)	1.31	325 (5.0)	1.69	0.78 (0.66–0.92)
eGFR 40% composite kidney outcome	848 (13.1)	4.80	995 (15.3)	5.66	0.84 (0.77–0.92)
Kidney failure	251 (3.9)	1.37	297 (4.6)	1.63	0.83 (0.70–0.98)
End-stage kidney disease	149 (2.3)	0.76	188 (2.9)	0.96	0.79 (0.64–0.98)
Sustained decrease in eGFR to <15 mL/min/1.73 m^2	192 (3.0)	1.05	237 (3.7)	1.30	0.80 (0.66–0.96)
Sustained ≥40% decrease in eGFR from baseline	811 (12.5)	4.59	962 (14.8)	5.47	0.83 (0.76–0.92)
Renal death	2 (<0.1)	0.01	4 (<0.1)	0.02	0.54 (0.10–2.93)
eGFR 57% composite kidney outcome	356 (5.5)	1.95	465 (7.2)	2.56	0.76 (0.66–0.88)
Sustained ≥57% decrease in eGFR from baseline	254 (3.9)	1.39	361 (5.6)	1.99	0.70 (0.59–0.82)



Heart failure

Finerenone was investigated in FINEARTS-HF, a randomised, double-blind, placebo-controlled, multicentre phase III study in adult patients with heart failure and a left ventricular ejection fraction (LVEF) ≥ 40%. In FINEARTS-HF, patients were enrolled who had been diagnosed with heart failure (NYHA class II–IV) and were being treated on an outpatient or inpatient basis primarily for heart failure with a documented left ventricular ejection fraction (LVEF) ≥ 40%. Further inclusion criteria were an eGFR ≥ 25 mL/min/1.73m^2 and a serum potassium level ≤ 5.0 mmol/L. All patients were already receiving standard therapy for heart failure, including diuretics.

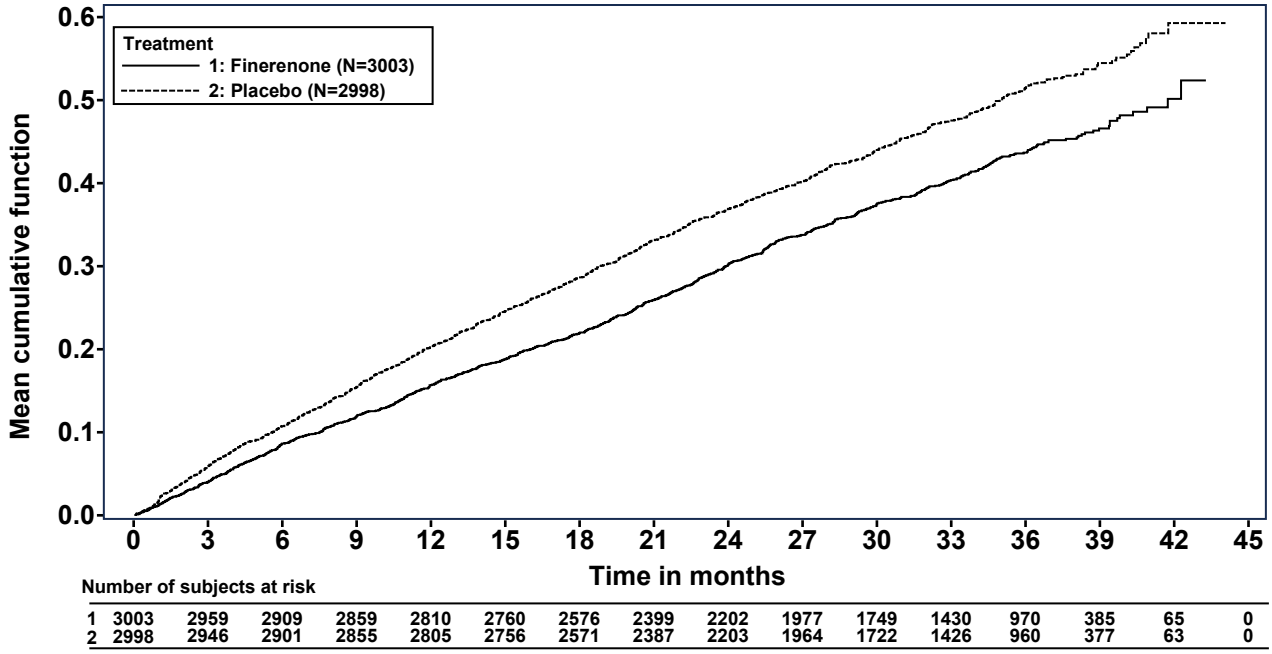
The primary endpoint of the FINEARTS-HF study was the composite of cardiovascular (CV) death and total (first and recurrent) heart failure events, comprised of hospitalisation for heart failure and urgent doctor visits for heart failure. Main secondary endpoints were total (first and recurrent) heart failure events, change from baseline to Month 6, 9 and 12 in Total Symptom Score (TSS) of the Kansas City Cardiomyopathy Questionnaire (KCCQ) (which quantifies heart failure symptom frequency and severity), improvement in NYHA class from study baseline to Month 12, and first occurrence of the composite renal endpoint (sustained [≥4-week] decrease in eGFR ≥50% from study baseline, or below 15 mL/min/1.73 m^2, or initiation of dialysis or renal transplantation), and time to all-cause mortality.
The study investigated 6001 patients randomly treated (1:1) with finerenone (n = 3003) or placebo (n = 2998). The individual dose was dependent on renal function (target dose of 20 mg for an eGFR ≥ 25 - < 60 mL/min/1.73 m^2 and 40 mg for an eGFR ≥ 60 mL/min/1.73 m^2) and the extent of the increase in serum potassium levels during finerenone treatment. After 24 months, dose distribution in the finerenone arm was as follows: 35% were receiving 40 mg once daily, 32% were receiving 20 mg once daily, 12% were receiving 10 mg once daily and 1% had interrupted treatment. Approximately 80% of the patients reached their target dose at any time during treatment.
The study included 3247 (54%) patients with a heart failure event in the past 3 months, including 1219 (20%) patients randomised during hospitalisation or within 7 days of discharge.
Median follow-up was 2.7 years. Vital status at study end was known for 99.7% of patients. The study population was 79 % white, 17 % Asian and 1.5 % black. Mean age at recruitment was 72 years and 46% of patients were women. Mean baseline LVEF was 53%, with 64% of patients having an LVEF ≥ 50%, and with 69% and 30% of patients categorised as NYHA class II and III, respectively. Mean blood pressure was 129/75 mmHg and mean body mass index (BMI) was 30 kg/m^2. The median NT-proBNP was 1041 pg/mL; mean eGFR was 62 mL/min/1.73m^2, with 48% of patients having an eGFR < 60 mL/min/1.73 m^2, and the median UACR was 18 mg/g. Atrial fibrillation was present in 38% of patients and 41% had type 2 diabetes mellitus. The majority of patients were being treated with loop diuretics (87%), an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin-receptor blocker (ARB) (79%), 9% were receiving an angiotensin-receptor neprilysin inhibitor (ARNI) and 14% SGLT2 inhibitors.
Finerenone significantly reduced the risk for the primary combined endpoint (RR 0.84, 95% CI 0.74–0.95, p = 0.0072; see Table 6 and Figure 6). The effect was observed early on, with event curves separating from the first month and continuing to diverge throughout the study period (see Figure 6).
Finerenone also demonstrated superiority to placebo on the secondary endpoints of total heart failure events (RR 0.82, 95% CI 0.71–0.94, p = 0.0062) and change in KCCQ-TSS from baseline to month 6, 9 and 12, which indicated improvements in symptom frequency and symptom burden (adjusted mean 1.56, 95% CI 0.79–2.34, p< 0.0001). A numerical benefit with finerenone versus placebo was demonstrated for time to all-cause mortality, but this endpoint did not achieve statistical significance (HR 0.93, 95% CI 0.83–1.06). The confirmatory secondary efficacy endpoints are listed in Table 6. The

treatment effect for the primary and relevant secondary endpoints was consistent across all pre-specified subgroups, including sex, LVEF, NYHA class, eGFR, time since latest heart failure event, SGLT2 inhibitor therapy and type 2 diabetes mellitus status.

Table 6: Analysis of the primary and secondary endpoints (and their individual components for time-to-event endpoints) in Phase III Study FINEARTS-HF

	Patients with Heart Failure and LVEF ≥ 40%					
	Finerenone 10 or 20 or 40 mg once daily n = 3003		*Placebo n = 2998*		*Treatment effect Finerenone/Placebo*	
Primary and secondary efficacy endpoints:	*[Event Total] n (%) {Least Squares Mean}*	*Event rate (100 PY)*	*[Event Total] n (%) {Least Squares Mean}*	*Event rate (100 PY)*	*Hazard Ratio (HR) Odds Ratio (OR) Rate Ratio (RR) LS Mean difference (LSM) [95% CI]*	*p-value*
Primary combined endpoint of CV death and total heart failure events	[1083] 624 (20.8%)	14.88	[1283] 719 (24.0%)	17.70	RR 0.84 [0.74; 0.95]	0.0072
Total heart failure events	[842] 479 (16.0%)	11.57	[1024] 573 (19.1%)	14.12	RR 0.82 [0.71, 0.94]	0.0062
CV death	242 (8.1%)	3.33	260 (8.7%)	3.59	HR 0.93 [0.78; 1.11]	-
Change from baseline in KCCQ-TSS	{7.99}	-	{6.43}	-	LSM 1.56 [0.79, 2.34]	< 0.0001
Improvement in NYHA class	557† (18.6%)	-	553 (18.4%)	-	OR 1.01 [0.88, 1.15]	0.9295*
* Not significant (testing procedure stopped) † N = 3002						

Figure 6: Primary combined endpoint of CV death and total heart failure events in Phase III study FINEARTS-HF



Pharmacokinetics

Absorption

Finerenone is almost completely absorbed after oral administration. Absorption is rapid, with peak plasma concentrations (C_{max}) reached 0.5 to 1.25 hours after tablet ingestion in the fasted state. The absolute bioavailability of finerenone is 43.5% due to first-pass metabolism in the intestinal wall and liver. Finerenone is not a substrate of the efflux transporter P-gp *in vivo*.
Intake with high-fat, high-calorie food increased finerenone AUC by up to 21%, reduced C_{max} by up to 23% and prolonged the time to reach C_{max} by up to 2.5 hours. This is not clinically relevant. Therefore, finerenone can be taken independently of meals (see section “Dosage/Administration”).

Distribution

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

Metabolism

Approximately 90% of finerenone metabolism is mediated by CYP3A4 and 10% by CYP2C8. Four major metabolites (M-1a, M-1b, M-2a and M-3a) were found in plasma. All metabolites are pharmacologically inactive.

Elimination

Finerenone elimination from plasma is rapid, with an elimination half-life ($t_{1/2}$) of about 2 to 3 hours. Excretion of unchanged finerenone represents a minor excretory pathway (< 1% of dose in the urine via glomerular filtration, < 0.2% in the faeces). About 80% of the administered dose was excreted via urine, and around 20% of the dose via faeces, almost exclusively in the form of metabolites. With a systemic clearance of about 25 L/h, finerenone can be classified as an active substance with low clearance.

Linearity/non-linearity

Finerenone pharmacokinetics is linear across the investigated dose range of 1.25 to 80 mg.

Kinetics in specific patient groups

Hepatic impairment

In cirrhotic patients with mild hepatic impairment (Child-Pugh A), no change in finerenone exposure was shown.
In cirrhotic patients with moderate hepatic impairment (Child-Pugh B), the mean AUC of finerenone was increased by 38% and C_{max} was unchanged compared to healthy control subjects (see section “Dosage/Administration”).
There are no data for patients with severe hepatic impairment (Child-Pugh C) (see sections “Dosage/Administration” and “Warnings and precautions”).

Renal impairment

Mild renal impairment (creatinine clearance (CL_{CR}) 60 to < 90 mL/min) had no influence on the AUC and C_{max} of finerenone. Compared to subjects 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 the AUC of finerenone was similarly high, with increases of 34–36%. Moderate or severe renal impairment had no effects on C_{max} (see section “Dosage/Administration”).
Due to the high plasma protein binding, finerenone is not expected to be dialysable.

Elderly patients

58% of the 2818 patients who received finerenone in the FIDELIO-DKD study were 65 years old or older and 15% were 75 years old or older. Overall, no differences in safety or efficacy were observed between these patients and younger patients.
53% of the 3671 patients who received finerenone in the FIGARO-DKD study were 65 years old or older and 14% were 75 years old or older. Overall, no differences in safety or efficacy were observed between these patients and younger patients.
79% of the 2993 patients who received finerenone in the FINEARTS-HF study were 65 years old or older and 43% were 75 years old or older. Overall, no differences in safety or efficacy were observed between these patients and younger patients.

Elderly patients (≥ 65 years) exhibited higher plasma concentrations of finerenone than younger patients (≤ 45 years), with mean AUC and C_{max} values being 34% and 51% higher in the elderly (see section ”Dosage/Administration”).

Body weight

In population pharmacokinetic analyses, body weight was shown to be a covariate for the C_{max} and AUC of finerenone, leading to higher finerenone C_{max} and AUC values in subjects with lower body weight and lower finerenone C_{max} and AUC values in subjects with higher body weight. C_{max} and AUC of patients with a body weight below 57 kg were estimated to be, on average, 52% and 30% higher, respectively, and in patients with a body weight above 122 kg, 32% and 20% lower, respectively, than in a patient between 57 and 122 kg. Dose adjustment based on body weight is not required (see section “Dosage/Administration”).

Preclinical data

Non-clinical data reveal no special hazard for humans at clinically relevant concentrations for humans, based on conventional studies to assess safety pharmacology, acute toxicity and phototoxicity.
Effects observed in repeat-dose toxicity studies were mainly due to exaggerated pharmacodynamic activities of finerenone and secondary adaptive responses.

Reproductive toxicity

In rats, male fertility was not influenced by doses of up to 30 mg/kg/day finerenone (6 times (40 mg dosage) and 16 times (20 mg dosage) the $AUC_{unbound}$ in humans). Finerenone caused reduced fertility in female rats (reduced number of corpora lutea and implantation sites), as well as signs of early embryonic toxicity (increased post-implantation losses and reduced number of viable fetuses) at about 9 times the $AUC_{unbound}$ in humans for the 40 mg dosage and about 21 times the $AUC_{unbound}$ in humans for the 20 mg dosage. Furthermore, reduced ovarian weights were found at about 7 times the human $AUC_{unbound}$ for the 40 mg dosage and about 17 times the human $AUC_{unbound}$ for the 20 mg dosage. At 4 times the human $AUC_{unbound}$ for the 40 mg dosage and at 10 times the human $AUC_{unbound}$ for the 20 mg dosage, no effects on female fertility and early embryonic development were observed.
In the embryofetal toxicity studies in rats, oral administration of finerenone led to reduced placental weight and signs of embryofetal toxicity, including reduced fetal weight and delayed ossification at the maternally toxic dose of 10 mg/kg/day and more. This was equivalent to an $AUC_{unbound}$ 7 times (40 mg dosage) and 19 times (20 mg dosage) above clinical exposure. At 30 mg/kg/day, the incidence of visceral and skeletal variations was increased (mild oedema, shortened umbilical cord, slightly enlarged fontanelle) and one fetus showed complex malformations, including a rare malformation (double aortic arch). $AUC_{unbound}$ is about 10 times above clinical exposure at the 40 mg dosage and about 25 times above clinical exposure at the 20 mg dosage. The NOAEL of 3 mg/kg/day (low dose) in rats revealed a safety margin equivalent to 4 times the $AUC_{unbound}$ at the 40 mg dosage and 10 times at the 20 mg

dosage. In rabbits, the NOAEL of 2.5 mg/kg/day (high dose) revealed a safety margin equivalent to 5 times (40 mg dosage) and 13 times (20 mg dosage) the $AUC_{unbound}$, respectively.
In the pre- and postnatal development study in rats, increased pup mortality and other adverse findings (lower pup weight, delayed pinna unfolding) were observed at a dosage of 3 mg/kg/day or more. In addition, the pups in this dose group showed slightly increased locomotor activity, but no other neurobehavioural changes starting from an $AUC_{unbound}$ roughly 2 times above clinical exposure at the 40 mg dosage or 4 times above clinical exposure at the 20 mg dosage. The NOAEL of 1 mg/kg/day revealed a safety margin roughly equivalent to twice the $AUC_{unbound}$ for the 20 mg dosage and is within the therapeutic range for the 40 mg dosage. The increased locomotor activity in offspring might indicate a potential risk for the fetus.

Genotoxicity

Finerenone did not induce mutations in the bacterial mutagenesis assay (Ames test). *In vitro*, finerenone induced no chromosomal aberrations in Chinese hamster V79 lung cells. In the micronucleus test in male mice *in vivo*, intraperitoneal finerenone at concentrations of up to 1000 mg/kg/day were not clastogenic. Overall, finerenone showed no genotoxic potential.

Carcinogenicity

In 2-year carcinogenicity studies, oral administration of finerenone did not show any carcinogenic potential in male and female rats or in female mice. In male mice, finerenone led to an increase in Leydig cell adenomas at a dose of 30 mg/kg/day, which is equivalent to an $AUC_{unbound}$ 10-26 times above clinical exposure. A dose of 10 mg/kg/day, which was equivalent to an $AUC_{unbound}$ 7 times above clinical exposure for the 40 mg dosage and 17 times above clinical exposure for the 20 mg dosage, caused no tumors. Based on the known sensitivity of rodents to develop these tumors, as well as the pharmacology-based mechanism at supratherapeutic doses and the adequate safety margins, the increase in Leydig cell tumors in male mice is not deemed clinically relevant.

Other information

Shelf life

Do not use this medicine after the expiry date marked as “EXP” on the pack.

Special precautions for storage

Keep out of the reach of children.
Do not store above 30°C.
Store in the original packaging.

Authorisation number

68130 (Swissmedic).

Packs

10 mg film-coated tablets: Packs of 28 or 98 film-coated tablets (B)

20 mg film-coated tablets: Packs of 28 or 98 film-coated tablets (B)

40 mg film-coated tablets: Packs of 28 or 98 film-coated tablets (B)

Marketing authorisation holder

Bayer (Schweiz) AG, Zurich

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November 2025