FINERENONE tablets (Kerendia® ▼)
for treating chronic kidney disease (CKD) in type 2 diabetes

The Cheshire and Merseyside Area Prescribing Group recommends the prescribing of FINERENONE tablets (Kerendia® ▼), for treating chronic kidney disease (CKD) in type 2 diabetes in accordance with NICE TA877.

AMBER following specialist initiation

NICE technology appraisal (TA) 877[1] recommends finerenone as an option for treating stage 3 and 4 chronic kidney disease (with albuminuria) associated with type 2 diabetes in adults only if:

- It is an add on to optimised standard care. This should include, unless they are unsuitable, the highest tolerated doses of:
  - angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs), **and**
  - sodium-glucose cotransporter-2 (SGLT2) inhibitors, **and**
- people have an estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73m^2 or more[1]

Costing information

The cost-effectiveness estimates are uncertain, but they are all within the range that NICE considers an acceptable use of NHS resources. Because finerenone has not been compared directly with SGLT2 inhibitors as an add-on to standard care (without SGLT2 inhibitors), it cannot be recommended instead of them. So, finerenone is recommended as an add-on to standard care, when standard care includes SGLT2 inhibitors.[1]

NICE does not expect this guidance to have a significant impact on resources; that is, the resource impact of implementing the recommendations in England will be less than £5 million per year (or approximately £9,000 per 100,000 population).[2]

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

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Effectiveness

Finerenone is a nonsteroidal, selective mineralocorticoid receptor antagonist.[3]

The clinical effectiveness evidence for finerenone was from the phase 3, randomised, double-blind, multicentre, placebo-controlled trial, **FIDELIO-DKD** [4], designed to test the hypothesis that finerenone slows CKD progression and reduces cardiovascular mortality among patients with advanced CKD and type 2 diabetes. The trial enrolled over 5000 adults with CKD and type 2 diabetes who took 10mg or the target 20mg dose once daily or placebo, in addition to standard care. The inclusion criteria included an albumin to creatinine ratio of 3.4 mg/mmol to less than 33.9 mg/mmol, an eGFR of 25 ml/min/1.73 m^2 to <60 ml/min/1.73 m^2, and diabetic retinopathy, or an albumin to creatinine ratio of 33.9 mg/mmol to 565 mg/mmol, and an eGFR of 25 ml/min/1.73 m^2 to <75 ml/min/1.73 m^2. The primary composite endpoint was kidney failure, a sustained decrease of at least 40% in eGFR from baseline or death from renal causes. The secondary composite endpoint was death from cardiovascular causes. During a median follow-up of 2.6 years, a primary outcome event occurred in 504 of 2833 patients (17.8%) in the finerenone group and 600 of 2841 patients (21.1%) in the placebo group (95% CI 0.73 to 0.93; P=0.001). A key secondary outcome event occurred in 367 patients (13.0%) and 420 patients (14.8%) in the respective groups (95% CI, 0.75 to 0.99; P=0.03). Overall, the frequency of adverse events was similar in the two groups. The incidence of hyperkalemia-related discontinuation of the trial regimen was higher with finerenone than with placebo (2.3% and 0.9%, respectively). The placebo-corrected relative reduction in urinary-albumin-to-creatinine ratio (UACR) in patients randomised to finerenone was 31% at month 4. The trial concluded that patients with CKD and type 2 diabetes, treatment with finerenone resulted in lower risks of CKD and cardiovascular events than placebo.[4]

Safety[3]

Refer to SPC for full safety information.

Drug interactions/contraindications: Finerenone is contraindicated in hypersensitivity to the active substance or to any of the excipients listed in the SPC, concomitant treatment with strong inhibitors of CYP3A4 including itraconazole, ketoconazole, ritonavir, nelfinavir, cobicistat, clarithromycin, telithromycin, nefazodone, and in Addison's disease.

Use in caution with potassium supplements, trimethoprim or trimethoprim/sulfamethoxazole. Temporary discontinuation may be necessary. See **Patient factors**.

Hyperkalaemia: Hyperkalaemia has been observed in patients treated with finerenone. Risk factors include low eGFR, higher serum potassium and previous episodes of hyperkalaemia. Local guidelines for the management of hyperkalaemia must be followed. The risk of hyperkalaemia also may increase with the intake of concomitant medications that may increase serum potassium. See **Patient factors**.

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

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

Women of childbearing potential should be advised to use effective contraception during treatment with finerenone. Women should be advised not to breast-feed during treatment with finerenone.

Cost

The cost-effectiveness estimates are uncertain, but they are all within the range that NICE considers an acceptable use of NHS resources. As finerenone has not been compared directly with SGLT2 inhibitors as an add-on to standard care (without SGLT2 inhibitors), it cannot be recommended instead of them. So, finerenone is recommended as an add-on to standard care, when standard care includes SGLT2 inhibitors.[1]

The list price of finerenone is £36.68 for 28 tablets, for both the 10-mg and 20-mg doses.[5] The annual cost of treatment is £478.15. Costs may vary in different settings because of negotiated procurement discounts.

Patient factors[3]
Elderly: No dose adjustment is necessary in elderly patients.

Paediatric population: The safety and efficacy of finerenone in children and adolescents aged under 18 years have not yet been established.

Renal impairment: In patients with eGFR < 25 mL/min/1.73 m^2, finerenone treatment should not be initiated and discontinued if the patient progresses to end-stage renal disease during 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.

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 should not be initiated in patients with severe hepatic impairment.

No initial dose adjustment is required in patients with moderate hepatic impairment. Consider additional serum potassium monitoring and adapt monitoring according to patient characteristics.

No initial dose adjustment is required in patients with mild hepatic impairment.

Concomitant medication: Finerenone should not be given concomitantly with potassium sparing diuretics (e.g. amiloride, triamterene) or other mineralocorticoid receptor antagonists (e.g. eplerenone, spironolactone).

Additional serum potassium monitoring and adaptation of monitoring according to patient characteristics should be considered in patients taking finerenone concomitantly with moderate or weak CYP3A4 inhibitors, potassium supplements, trimethoprim, or trimethoprim/sulfamethoxazole.

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

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

Prescribing information[3]

- Finerenone tablets are for oral use. They may be taken with a glass of water and with or without food, but should not be taken with grapefruit or grapefruit juice.
- For patients who are unable to swallow whole tablets, tablets may be crushed and mixed with water or soft foods, such as apple sauce, directly before oral use.
- A missed dose should be taken as soon as the patient notices, but only on the same day.
- The maximum recommended dose is 20 mg finerenone once daily.

Initiation of treatment[3]

- Serum potassium and eGFR must be measured prior to initiation to determine if finerenone treatment can be started and to determine the starting dose. See table 1 below.
- The recommended starting dose of finerenone is based on eGFR. Finerenone treatment should not be initiated In patients with eGFR < 25 mL/min/1.73 m^2.
- If serum potassium ≤ 4.8 mmol/L, finerenone treatment can 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 > 5.0 mmol/L, finerenone treatment should not be initiated.

Table 1: Initiation of treatment and recommended dose[3]

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

Continuation of treatment[3]

- Remeasure serum potassium and eGFR 4 weeks after initiation, re-start of finerenone, or when the dose has been increased. See table 2 below.
- Thereafter, serum potassium must be measured periodically based on patient characteristics and potassium levels. **See Safety** and **Patient factors.**
- In patients with eGFR ≥ 15 mL/min/1.73 m^2, finerenone treatment can be continued with dose adjustment based on serum potassium. See table 2 below.
- Finerenone treatment should be discontinued in patients who have progressed to end-stage renal disease (eGFR < 15 mL/min/1.73 m^2).
- If serum potassium > 5.5 mmol/L, finerenone treatment has to be withheld. Local guidelines for the management of hyperkalaemia must be followed.

Table 2: Continuation of finerenone treatment and dose adjustment[3]

		Current finerenone dose (once daily)	
		10mg	**20mg**
Current serum potassium (mmol/L)	**≤ 4.8**	Increase to 20 mg finerenone once daily, unless eGFR has decreased > 30% compared to the previous measurement. Maintain 10mg once daily if eGFR has decreased > 30% compared to the previous measurement.	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.

Implementation notes

- Prescribing and monitoring of finerenone must be retained by the specialist until stabilisation of the dose is achieved and the patient has been reviewed by the specialist. The specialist may then request the patient's GP to take over prescribing responsibilities of treatment. The specialist clinician may be situated in hospital or within a locally commissioned consultant/GP specialist-led service situated in primary care.
- Serum potassium must be measured periodically based on patient characteristics and potassium levels**. See Safety** and **Patient factors.** The risk of hyperkalaemia increases with decreasing renal function. **[3]**
- Ongoing monitoring of renal function should be performed as needed according to standard practice**[3]** and consideration of patient factors.
- Prescribers should continue to follow NICE CKD guideline recommendations (NG203) in relation to which individuals require referral to a specialist.

- **Embryo-foetal toxicity**
  - Women of childbearing potential should be advised to use effective contraception during treatment with finerenone. [3]
  - It is the responsibility of the initiating prescriber (the specialist) to ensure that the patient is using effective contraception prior to commencing treatment, advised of the need to continue use during treatment, and is counselled appropriately. Confirmation that benefits, risks and contraception have been discussed and details of any action taken should be provided to primary care if primary care prescribing of contraception is requested.
  - 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. [3]
  - Patients should be advised not to breast-feed during treatment with finerenone.[3]

References

1. National Institute for Health and Care Excellence. Technology Appraisal 877; Finerenone for treating chronic kidney disease in type 2 diabetes, 23 March 2023. Accessed online 24 March 2023
2. National Institute for Health and Care Excellence. Technology Appraisal 877; Resource Impact Statement: Finerenone for treating chronic kidney disease in type 2 diabetes, 23 March 2023. Accessed online 24 March 2023
3. Bayer plc. Summary of product characteristics; Kerendia® ▼ 10mg film coated tablets. 7 March 2022. Accessed online 28 February 2023
4. Bakris et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. *NEJM*. 2020;383:2219-29. DOI: 10.1056/NEJMoa2025845
5. NHS Business Services Authority, dm+d browser. Accessed online 14 April 2023.