MANAGEMENT OF CHRONIC KIDNEY DISEASE ASSOCIATED WITH TYPE 2 DIABETES

Practical guidance and clinical pearls

This promotional document was developed and funded by Bayer.

The document is designed to support UK HCPs with the optimisation of the management of patients who have a diagnosis of Chronic Kidney Disease (CKD) associated with Type 2 Diabetes (T2D) in a primary care setting. It is not intended to replace clinical judgement. When making clinical decisions please take into consideration the individual medicines relevant SmPC.

In the United Kingdom, Finerenone▼ is indicated for the treatment of chronic kidney disease (stage 3 and 4 with albuminuria) associated with type 2 diabetes in adults[1].
For further information on dosing, special warnings and precautions for use of finerenone see page 5 of this document.

Adverse event reporting and Prescribing Information for Kerendia® ▼(finerenone) is available via the QR code on the right.
Either click here or scan the QR code for adverse event reporting information and prescribing information.

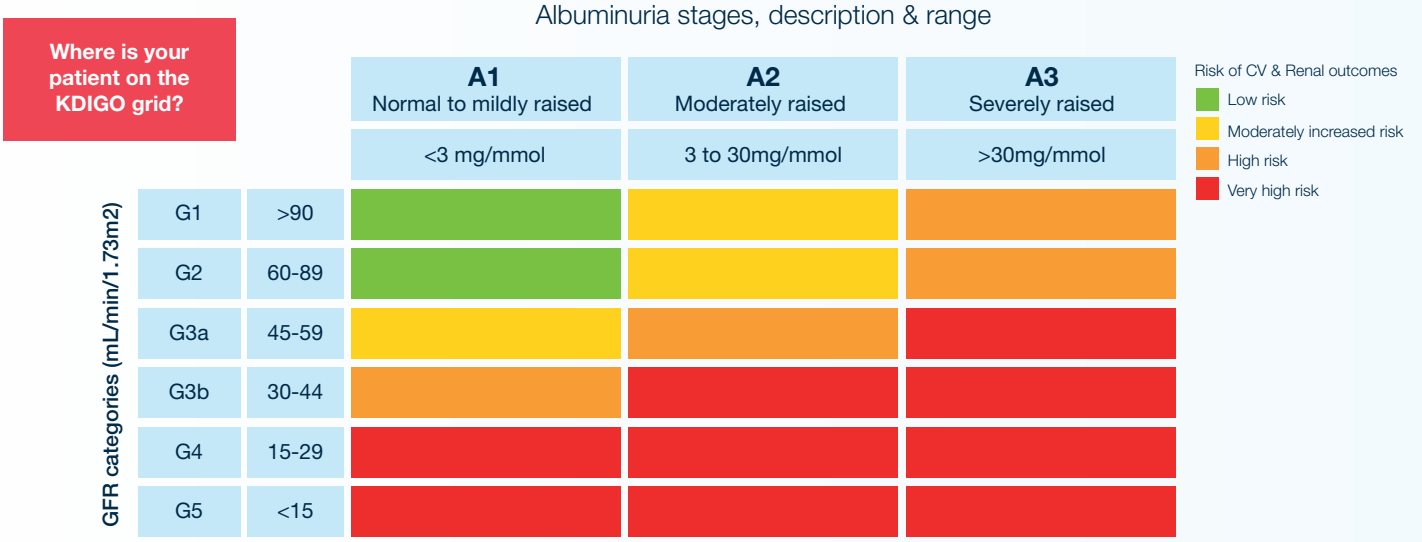
For direct access to this prescribing information, please ensure that your device's browser settings have automatic PDF download enabled.

Annual health check: Know your numbers

As part of their annual check, patients with diabetes should have at least the following checked[2]:

- Blood pressure
- UACR & eGFR
- Review HbA1c
- Review blood glucose control
- Cholesterol
- Eye screening
- Foot check
- Height & Weight

Risk of adverse outcomes in adults by eGFR & UACR category[3]



Prognosis of CKD by GFR and Albuminuria category

Referral criteria for adults with CKD for specialist assessment[4]

Refer adults with CKD for specialist assessment (taking into account their wishes & comorbidities) if they have any of the following:

- A 5 year risk of needing renal replacement therapy >5% (measured using the 4-variable KFRE)
- UACR ≥70mg/mmol, unless known to be caused by diabetes and already managed appropriately
- UACR >30mg/mmol (A3), together with haematuria
- A sustained decrease in eGFR of ≥25% and a change in eGFR category within 12 months
- A sustained decrease in eGFR of ≥15mL/min per year
- Hypertension that remains poorly controlled (above the person's individual target) despite the use of at least 4 antihypertensive medicines at therapeutic doses
- Known or suspected rare / genetic causes of CKD
- Suspected renal artery stenosis

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Manage cardiovascular (CV) risk factors

Lifestyle advice | Control Blood Pressure | Control Lipids | Improve Diabetic Control

Standardised diabetes management

Primary Care CKD in adults with T2DM treatment intensification Pathway

Know Your Numbers - CHECK eGFR & uACR

Pillar 1 — **ACEi/ARB**

UACR ≥3mg/mmol

Offer ACEi/ARB

Titrate to highest licensed dose that a person can tolerate[5]

QOF 2024/25 DM006[7]
The percentage of patients with diabetes, on the register, with a diagnosis of nephropathy (clinical proteinuria) or micro-albuminuria who are currently treated with an ACE-I (or ARBs) 3 points, 57-97% threshold

+

Pillar 2 — **SGLT2i**

UACR ≥3mg/mmol
+ Pillar 1

UACR 3-30 mg/mmol:
Consider SGLT2i if criteria met and within licence[5]**, unless unsuitable**

UACR >30 mg/mmol:
Offer SGLT2i if criteria met and within licence[5]**, unless unsuitable**

Given the variability in SGLT2i licenses, always refer to the relevant SmPC before prescribing

+

Pillar 3 — **Kerendia**

UACR ≥3mg/mmol
eGFR ≥25 - <60ml/min/1.73m²
+ Pillar 1 + Pillar 2

Offer Kerendia if in line with NICE recommendation and within licence[6]

+ Pillar 1

Offer Kerendia if patient is contraindicated, unsuitable for, or intolerant of SGLT2i if in line with NICE recommendation and within licence[6]

This list not exhaustive and is taken from a consensus statement from UK clinicians, funded and organised by Bayer plc[8]

Contraindicated to SGLT2i
- Hypersensitivity to active ingredients

Unsuitable for SGLT2i's
Possible reason a patient should not receive an SGLT2i
- History of unprovoked diabetic ketoacidosis
- Patients with rapid progression to insulin (within 12 months of T2D diagnosis
- History of recurrent mycotic genital infections
- Urinary sepsis resulting in recurrent hostpital admissions
- History of Fournier's gangrene
- Pancreatic disease

Intolerant of SGLT2i after an initial trial
Possible reason for discontinuation:
- Recurrent genital infections
- Patients who suffer symptomatic hypotension on an SGLT2i
- Urinary symptoms (frequency and recurrent infections)
- Indiosyncratic adverse events

Please refer to relevant SGLT2i SmPC before prescribing

T2DM, type 2 diabetes mellitus; ACEi, Angiotensin converting enzyme Inhibitor; ARB, Angiotensin receptor blocker; CKD, chronic kidney disease; CYP3A4, cytochrome P450 3A4; CYP2C8, cytochrome P450 2C8; eGFR, estimated glomerular filtration rate; HbA1c, Glycated haemaglobin; KDIGO, kidney disease improving global outcomes; KFRE, kidney failure risk equation; od, once daily; SGLT2i, sodium glucose co-transproter-2 inhibitor; SmPC, summary of product characteristics; T2D, type 2 diabetes; uACR, Urine albumin creatinine ratio

Scan or click the QR code to access Bayer's 'Testing and Pharmaceutical Management' infographic

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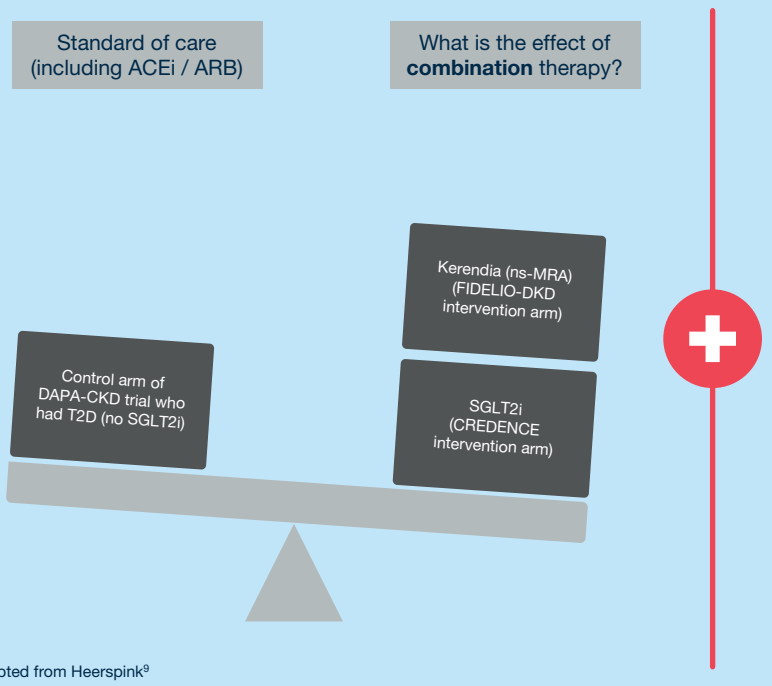
Heerspink study: Estimated lifetime benefit of pharmacological therapies in patients with type 2 diabetes and chronic kidney disease: A joint analysis of randomized controlled clinical trials[9]

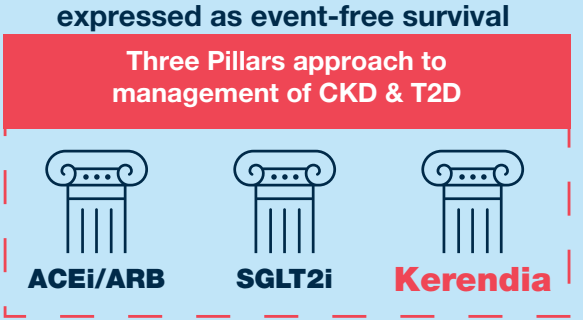
Combined disease-modifying treatment with an SGLT2 inhibitor and a ns-MRA in patients with type 2 diabetes and CKD **may substantially increase the number of years free from kidney failure and mortality**



Adapted from Heerspink[9]

- Cumulative effect using trial level data was estimated for Canagliflozin* & Kerendia
- This was compared to effects in the placebo arm of the DAPA-CKD study
- The primary outcome was a composite of doubling of serum creatinine, end stage kidney disease or death from kidney failure
- Risk of hyperkalaemia
- Due to limited data finerenone should be discontinued if eGFR <15ml/min/1.73m^2

Primary composite kidney outcome expressed as event-free survival



Study Design

Objective: Assess the cumulative effect of SGLT2 inhibitors and MRA compared with conventional therapy (ACE inhibitors or ARB) in patients with type 2 diabetes and CKD.

Methodology: Analysis of overall trial-level estimates from pivotal placebo-controlled randomized clinical trials. Inclusion criteria: Pivotal phase 3 clinical trials enrolling patients with type 2 diabetes and CKD, demonstrating significant risk reduction in primary kidney outcomes.

Included Trials: CREDENCE, FIDELIO-DKD and DAPA-CKD

Observational cohort study for robustness assessment: Chronic Renal Insufficiency Cohort (CRIC) Study.

Key Points:
- All participants provided written consent.
- Each trial and the CRIC Study was approved by the institutional review board at each site.
- Data from clinical trials and an observational study utilized to validate the efficacy and safety of the treatment.

***Canagliflozin is not licensed for use in CKD in the UK. Bayer does not encourage the use of any medicine out of its licensed indication, please refer to the SmPC for more information about the use of any medicine.**

SGLT2i, sodium-glucose cotransporter-2 inhibitor; Ns-MRA, nonsteroidal mineralocorticoid receptor antagonist; MRA, mineralocorticoid receptor antagonist

Scan or click the QR code to access Bayer's 'FIDELIO-DKD: Effect of finerenone on CKD Outcomes in T2D' infographic

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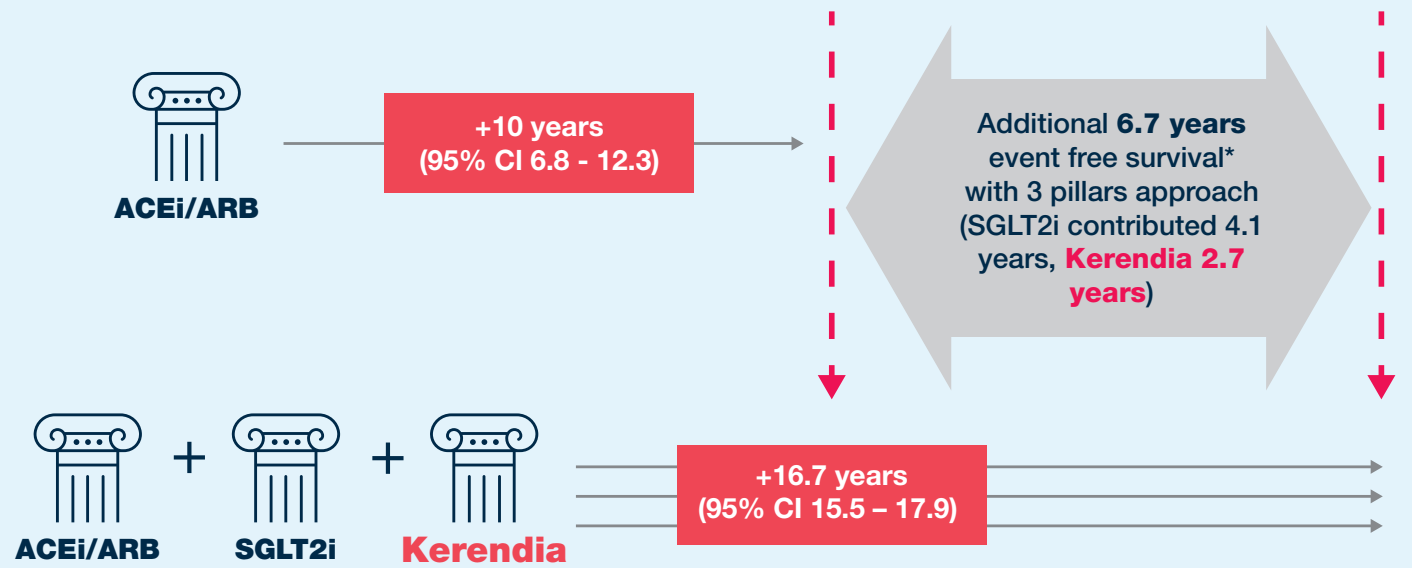
Heerspink study: Estimated lifetime benefit of pharmacological therapies in patients with type 2 diabetes and chronic kidney disease: A joint analysis of randomized controlled clinical trials[9]

According to the study an additional 6.7 years of event free survival could be provided for a 50-year-old when applying the 3 pillars approach to treatment.



What would an extra 6.7 years of event free survival mean to your patients?

***Primary outcome:** Composite of doubling of serum creatinine, end stage kidney disease or death from kidney failure

Adapted from Heerspink[9]

Study Limitations

Assumption of Incremental Benefits: Heerspink et al, relies on the presumption that individual therapies provide additional clinical benefits, potentially ignoring unknown pathways that could overlap between treatments.

Potential Overestimation of Effects: Early discontinuation of the CREDENCE and DAPA-CKD trials may lead to overestimation of treatment effects.

Constant Effect Assumption: Assumes treatments maintain a consistent effect over a lifetime, with no long-term efficacy data to confirm sustained benefits or account for changes in adherence.

Exclusion of Adverse Events and Costs: Focuses on kidney outcomes, cardiovascular outcomes, and mortality without evaluating the associated adverse events and treatment costs.

Risk of Overestimating Event-Free Survival: Possible overestimation due to not accounting for the competing risk of death, despite the significant reduction in overall mortality providing a survival advantage.

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Finerenone Initiation Considerations and Dosing Guidance[1]

Contraindications to the use of finerenone: Addison's disease, hypersensitivity to the active substance or excipients and concomitant treatment with strong CYP3A4 inhibitors. Please see the summary of product characteristics for further information.

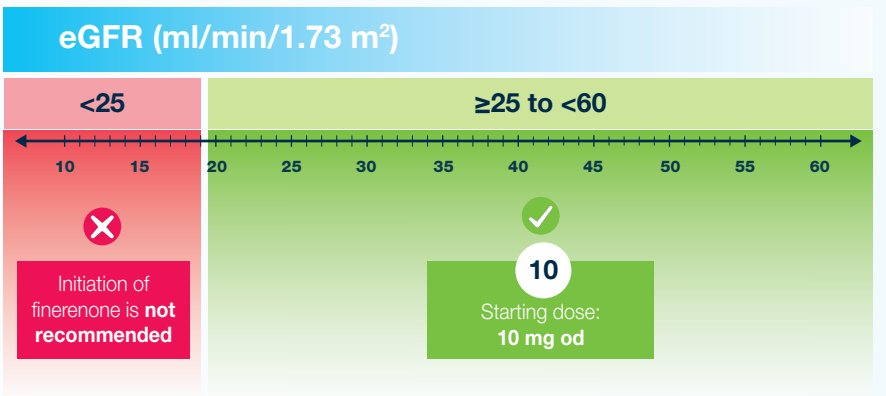
Initiating Treatment

Measurement of Serum Potassium Level & eGFR

- Serum potassium levels & eGFR have to be measured to determine whether patients can initiate finerenone
- The recommended starting dose of finerenone is 10mg od

Serum potassium levels	
mmol/l	Initiation of finerenone
≤4.8	✓ Can be started
>4.8 - 5.0	✓ May be considered*
>5.0	✗ Not recommended

*Initiation of finerenone may be considered with additional serum potassium monitoring within the first 4 weeks based on patient characteristics & serum potassium levels



Continuation of Treatment & Dose Adjustment

- Serum potassium & eGFR have to be re-checked 4 weeks after:
  - Initiation of treatment
  - Restarting treatment
  - An increase in dose
- Thereafter, serum potassium should be re-measured periodically & as needed based on patient characteristics & serum potassium levels
- Due to limited data finerenone should be discontinued if eGFR <15ml/min/1.73m^2

The recommended target dose & maximum dose of finerenone is 20 mg od

Current serum potassium (mmol/l)	Current finerenone dose	
	10 mg od	20 mg od
≤4.8	10 → 20: Increase dose to 20 mg od*	20 → 20: Maintain 20 mg od
>4.8 - 5.0	10 → 10: Maintain 10 mg od	20 → 20: Maintain 20 mg od
>5.0	10 → ✋: Withhold treatment. Consider restarting at 10 mg od when serum is potassium ≤5.0 mmol/L	20 → ✋: Withhold treatment. Restart at 10 mg od when serum potassium is ≤5.0 mmol/L

*Maintain 10 mg od if eGFR has decreased by >30% compared with the previous measurement

Key warning & Precautions: Hyperkalaemia has been observed in patients treated with Kerendia. The decision to initiate or continue treatment & adjust dose of kerendia should be based on serum potassium levels. Some patients are at a higher risk of hyperkalaemia, including those with a low eGFR, higher serum potassium & a history of hyperkalaemia. More frequent monitoring has to be considered in these patients. **Hepatic impairment:** No dose adjustment required in mild & moderate hepatic impairment. No data in severe hepatic impairment & treatment should not be initiated.
Interactions: Kerendia is cleared by CYP3A4 (90%) & CYP2C8 (10%), therefore it is important to note drug reactions with certain inhibitors & inducers of CYP3A4. Kerendia is contraindicated with strong CYP3A4 inhibitors (e.g. ketoconazole, ritonavir, nelfinavir, cobocistat, telithromycin, nefazodone) Concomitant use is not recommended with strong & moderate CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, St John's wort, efavirenz. Additional drug interactions include potassium sparing diuretics, other MRAs, potassium supplements & trimethoprim.

Consult SmPC for further details

eGFR, estimated glomerular filtration rate; OD, once a day

References: 1. Finerenone SmPC; Finerenone SmPC 10 & 20mg 2. Diabetes UK www.diabetes.org.uk Accessed Dec 2024; 3. KDIGO Diabetes Work Group. Kidney Int 2020; 98(4S):S1-115; 4. NICE CKD guidelines (NG203) last updated Nov 2021; 5. NICE guidelines: Type 2 diabetes in adults: Management (NG28) last updated June 2022; 6. NICE, Finerenone for treating chronic kidney disease in type 2 diabetes. Technology appraisal guidance [TA877]. March 2023; 7. Quality and Outcomes Framework 2024/25 Publication reference: PRN01104; 8. HCP consensus on SGLT2i unsuitability and intolerance Data on file (PP-KER-GB-0645); 9. Heerspink, H. et al Diabetes Obes Metab. 2023;1-10.