National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Finerenone for treating chronic kidney disease in people with type 2 diabetes

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness *It is important that appropriate topics are referred to NICE to ensure that NICE guidance is relevant, timely and addresses priority issues, which will help improve the health of the population. Would it be appropriate to refer this topic to NICE for appraisal?*	Bayer	It is appropriate to refer this topic to NICE for appraisal. Chronic kidney disease (CKD) is one of the most common diseases worldwide (1). Diabetes is the leading cause of CKD (2) with approximately half of CKD cases associated with diabetes (2). CKD affects approximately 38% of type 2 diabetes (T2D) patients (3). CKD in patients with T2D is a progressive disease associated with increased kidney and cardiovascular (CV) mortality (4). The risk of kidney and CV complications increases as patients progress to more advanced CKD stages (5). CKD in patients with T2D is associated with lower quality of life (QoL) compared to patients with T2D without CKD (6). CKD in patients with T2D is associated with a considerable economic burden, with the cost per patient significantly higher than for CKD or T2D alone (7). The medical resource utilisation and associated costs increase as patients progress to more advanced CKD stages (8). ACEi and ARB have been the mainstay treatment for retarding the progression toward end-stage renal disease for decades (9). Despite this, patients have a	Thank you for your comment.

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		residual risk of progression to more advanced CKD stages. Proven treatment alternatives are needed to reduce the burden among patients with CKD and T2D. Finerenone has been studied in a large population of patients with CKD and T2D and has demonstrated significant benefits on both renal and CV outcomes (10). (1) Jager, K.J., et al.,, *A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases.* Kidney Int, 2019. 96(5): p. 1048-1050., 2019. **96**(5) (2) Tuttle, K.R., et al., *Clinical Characteristics of and Risk Factors for Chronic Kidney Disease Among Adults and Children: An Analysis of the CURE-CKD Registry.* JAMA Netw Open, 2019. **2**(12): p. e1918169. (3) Wu B, Bell K,Stanford A,et al.Understanding CKD among patients with T2DM:prevalence, temporal trends,and treatment patterns—NHANES 2007–2012.BMJOpen Diabetes Research and Care 2016;4:e000154. (4) Afkarian M et al. Kidney Disease and Increased Mortality Risk in Type 2 Diabetes. J Am Soc Nephrol24: 302–308, 2013. (5) Kidney Disease: Improving GlobalOutcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for theEvaluation and Management of Chronic Kidney Disease.Kidney inter., Suppl.2013;3: 1–150. (6) Grandy S, et al. Change in health status (EQ-5D) over 5 years among individuals with and without type 2 diabetes mellitus in the SHIELD longitudinal study. Health Qual Life Outcomes 2012;10:99. (7) United States Renal Data System. 2019 Annual Data Report. Executive summary. (8) Nichols, G.A., et al., Health Care Costs by Type of Expenditure across eGFR Stages among Patients with and without Diabetes, Cardiovascular Disease, and Heart Failure. J Am Soc Nephrol, 2020 (9) Viazzi et al. Renin–angiotensin–aldosterone system blockade in chronic kidney disease: current strategies and a look ahead. Intern Emerg Med (2016) 11:627–635 (10) Bakris et al. Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes. N Engl J Med 2020; 383:2219-2229	
	Primary Care Diabetes Society	The draft remit is appropriate	Thank you for your comment.

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	Kidney Care UK	Yes	Thank you for your comment.
Wording *Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider? If not, please suggest alternative wording.*	Bayer	The wording of the remit is appropriate.	Thank you for your comment.
	Primary Care Diabetes Society	The wording of the remit is appropiate	Thank you for your comment.
	Kidney Care UK	Yes	Thank you for your comment.
Timing Issues	Bayer	Any intervention which will reduce pressure on NHS services, considering the inevitable backlog as a result of the COVID-19 pandemic, could be considered a priority. By reducing important and costly CV and renal events and delaying progression of CKD in T2D, finerenone would be a timely addition to the treatment options available to clinicians and patients in the NHS. Prevention is at the heart of the NHS Long Term Plan. CVDPREVENT is a National Primary Care audit commissioned by NHS England and NHS Improvement. The audit will target six common high-risk conditions that are linked to patients developing CV disease, one being CKD. The programme will support primary care in understanding how many patients with these high-risk conditions are undiagnosed, under treated or over treated. The audit will enable practices and primary care networks to systematically identify individuals whose clinical risk factors are sub-optimally managed so that they can be offered treatment to minimise their risk of a life-changing CV event.	Thank you for your comment. This topic has been scheduled into the work programme.

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		The standard of care for patients with CKD and T2D is limited to the use of renin-angiotensin blockage (ACEi/ARB) as well as optimising glucose control. Healthcare professionals will need access to a range of treatment class options to meet the needs of different patients identified for additional interventions for CKD in T2D. https://www.england.nhs.uk/ourwork/clinical-policy/cvd/cvdprevent/	
	Primary Care Diabetes Society	There is no immediate urgency of this appraisal to the NHS as RAS inhibition and SGLT2 inhibitors are already established therapeutic options for DKD and the latter have yet to be clearly embedded as standard of care of DKD	Thank you for your comment. This topic has been scheduled into the work programme.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Bayer	We would like to highlight a minor point. In terms of the size of the population, Bayer note that the reference for the size of the population of patients with diabetes in England relates to all those with diagnosed diabetes, not specifically T2D. The same statistics section of the referenced website refers to 90% of patients with diabetes having T2D, so Bayer consider the number quoted should be reduced to approximately 3 million. As stated in the background, NICE clinical guideline 182 recommends blood pressure targets for people with CKD and diabetes, and recommends a renin-	Thank you for your comment. The size of the population with type 2 diabetes has been updated. The wording related to pharmacotherapy for chronic kidney disease (CKD) reflects the recommendations in

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		angiotensin system antagonist., such as an ACE inhibitor or ARB for control of blood pressure if there is an ACR of 3 mg/mmol or more. Bayer suggest the wording could be amended here to reflect that a number of renin–angiotensin system antagonists are indicated - as part of an antihypertensive regimen - for the treatment of renal disease in adult patients with hypertension and T2D.	NICE clinical guideline 182 (which includes a recommendation to not offer a combination of renin-angiotensin system antagonists to people with CKD) and has not been updated.
	Primary Care Diabetes Society	Background info should contain more information specific to the prevalence of diabetic kidney disease (DKD) Diabetic kidney disease is the single most common cause of renal failure in adults starting renal replacement therapy in the UK (Nephron 2018;139(suppl1):13–46 DOI: 10.1159/000490959) UK National Diabetes Audit (2014): 42.3% of those with T2D were recorded as having renal disease (Hill CJ et al. Diabet Med 31:448–454 doi: 10.1111/dme.12312) Diabetes worsens all outcomes of CKD cf. those with CKD but without diabetes (Foley RN et al. J Am Soc Nephrol 16: 489-495, 2005. doi: 10.1681/ASN.2004030203)	Thank you for your comment. The background section of the scope is intended to provide a broad overview of the disease and its expected management. Information relating to the prevalence of diabetic kidney disease is already included in the background section. No changes have been made to the scope.
	Kidney Care UK	The background information should include: • The significant cost burden of treatment options for end stage renal failure. • The burden of treatment and impact on quality of life for patients and their families.	Thank you for your comment. The background section has been updated to include information provided on

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		• That treatment for kidney failure is the second most expensive complication of type 2 diabetes https://www.ncbi.nlm.nih.gov/pubmed/26773733 The increased risk of early death amongst people with diabetes and kidney disease (Diabetic kidney disease shortens lifespan by 16 years compared to diabetes or CKD alone – Wen Kidney Int. 2017 Aug;92(2):388-396) • That awareness of kidney disease as a complication of diabetes is low and particularly that rates of annual testing by GPs are low (Only 54% of people with diabetes are having the NICE recommended regular GP-based urine tests that can enable early identification of kidney disease (HQIP (2017) National Chronic Kidney Disease Audit, London.)	the impact on quality of life and the increased risk of early death amongst people with diabetes and kidney disease.
The technology/ intervention	Bayer	The description of the technology in the draft scope seems to imply that the effect of finerenone is on lowering blood pressure. Finerenone is a novel, nonsteroidal, selective mineralocorticoid receptor (MR) antagonist that has a high affinity for the MR and a unique binding mode that has been shown to reduce inflammation and fibrosis in animal models (1). Only modest reductions in blood pressure were observed in phase 2 studies (at the highest doses) and in the pivotal phase 3 study (FIDELIO-DKD) with finerenone (2,3). Haemodynamic effects have been observed in studies of dual renin-angiotensin system blockade that have not shown efficacy in delaying CKD progression, which supports a different mechanism of action for finerenone (3). There is growing evidence that pathophysiological MR overactivation leads to inflammation and fibrosis and is a key driver of CKD progression. Therefore,	Thank you for your comment. The technology section has been updated.

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		blockade of the MR is a potential novel treatment approach to slow the progression of CKD (1). (1) Agarwal R et al. Nephrol Diab Transplant (2020) 1-10 doi: 10.1093/ndt/gfaa294 (2) Bakris GL et al. JAMA. 2015;314(9):884-894. doi:10.1001/jama.2015.10081 (3) Bakris GL et al. N Engl J Med 2020; 383:2219-2229 DOI: 10.1056/NEJMoa2025845	
	Primary Care Diabetes Society	Finerenone is a non-steroidal MRA and has different pharmacokinetics and clinical effects to spironolactone and eplerenone, which are steroidal MRAs. Finerenone does not significantly lower blood pressure and has fewer steroid-induced adverse effects such as gynaecomastia, impotence and low libido. Finerenone has established anti-inflammatory and antifibrotic properties	Thank you for your comment. The technology section has been updated.
Population	Bayer	We would like to highlight a minor point. The term 'Chronic Kidney Disease (CKD)' should be used consistently throughout the documentation describing this appraisal instead of diabetic kidney disease.	Thank you for your comment. The population has been updated to 'adults with type 2 diabetes and chronic kidney disease'.
	Primary Care Diabetes Society	Adults with DKD with significant albuminuria >30mg/mmol and eGFR down to 25ml/min	Thank you for your comment. The population in the scope has been kept broad. The appraisal committee will be able to make

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			recommendations within the marketing authorisation for this technology.
	Kidney Care UK	Progression of CKD has been found to be more rapid in specific groups and it may be necessary to consider these groups separately. eg “Some ethnic groups, particularly Bangladeshi, appear to be more sensitive to the combined effects of proteinuria and hypertension than other ethnic groups. Also, clinicians need to be aware that younger people with diabetes (<55 years) with CKD are at twice the risk of rapid progression of CKD compared with those >65 years and thus need closer monitoring, management of risk factors and early specialist review to delay progression.” (Mathur R, Dreyer G, Yaqoob MM, et al Ethnic differences in the progression of chronic kidney disease and risk of death in a UK diabetic population: an observational cohort study BMJOpen 2018;8:e020145. doi: 10.1136/bmjopen-2017-020145)	Thank you for your comment. Subgroup analyses may be reported but this will depend on the availability of data. The appraisal committee will consider the relevance of subgroups (if the data allows this) but will only be able to make recommendations within the licensed marketing authorisation. This may also be considered a potential equality issue and is documented in the equalities impact assessment form for this appraisal. No changes have been made.

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Comparators	Bayer	When considering the most clinically relevant comparator for inclusion within an appraisal of the clinical and cost effectiveness of finerenone, Bayer refers to the NICE methods guide (1). Section 6.2.2 of the 'Guide to the methods of technology appraisal 2013' (1) states that the committee must consider the following five factors, when selecting the most appropriate comparator(s): • Established NHS practice in England • The natural history of the condition without suitable treatment • Existing NICE guidance • Cost-effectiveness • The licensing status of the comparator Additionally, section 6.2.3. states that the above five factors are not considered equally; rather, the committee will normally be guided by established practice in the NHS. When considering SGLT2i inhibitors as a comparator to finerenone, the five factors of section 6.2.2. have not been met. Only one SGLT2 inhibitor, canagliflozin, includes a reference in section 4.1 of the SmPC "therapeutic indications" to data on renal outcomes in subsequent sections of the SmPC. (13). The existing NICE guideline for the treatment and management of CKD makes no mention of SGLT2 inhibitors as part of the treatment pathway (3). Most importantly, sales data estimate the market share (by volume) of SGLT2 inhibitors at less than 6% as compared against oral and parenteral hypoglycaemics (2). The guiding principle for comparator selection of section 6.2.3, has not been met. SGLT2 inhibitors do not represent part of established practice in the NHS. As such, comparison should not be made either against the class or any particular SGLT2 inhibitor.	Thank you for your comment. In order to keep the scope inclusive at this early stage, SGLT2 inhibitors have been retained. The company will have the opportunity to outline its rationale to committee for the comparators it considers to be most relevant within its submission.

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		The mode of action of the two classes of drugs are different and there are key differences in trial methodology and patient populations between the FIDELIO-DKD trial and the recent studies of SGLT2 inhibitors in CKD patients that would limit the suitability and quality of such a comparison. The rationale for Bayer's position on these issues is set out in the four subsections below. **1: Are SGLT2 inhibitors part of established NHS practice in England for treating CKD patients with type 2 diabetes?** It is recognised in the methods guide that whilst the five factors of 6.2.2 should be considered, they are normally not considered equally. Rather, the committee will normally have their decision be "guided by established practice in the NHS when identifying the appropriate comparator(s)" (1). Sales data for SGLT2 inhibitors show, when compared against oral and parenteral hypoglycaemics, that they are not sufficiently prescribed to represent part of routine care for patients with diabetes (less than 6% of volume) (2). Further, it is not known what proportion of this low volume is for patients with both type 2 diabetes and CKD. For SGLT2 inhibitors to form current best practice within the NHS, it would be expected that this would be reflected in current NICE guidelines for the indication in question. As set out in subsection 2, this is not the case. Bayer also recognise, as specified in subsection 6.2.4 of the methods guide, that the committee is not restricted to consider only those therapies with a marketing authorisation in the defined indication. Understanding this, it should be noted that only one SGLT2 inhibitor, canagliflozin, includes a reference in section 4.1 of the SmPC "therapeutic indications" to data on renal outcomes in subsequent sections of the SmPC (13). As above, sales estimates show that it cannot reasonably be stated, whilst licensed or unlicensed, that SGLT2	

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		inhibitors represent an established part of clinical practice for the treatment of CKD patients with diabetes. **2: Does any existing NICE guidance recommend SGLT2 inhibitors for the treatment of CKD patients with type 2 diabetes?** The current published guideline for this indication '*Chronic kidney disease in adults: assessment and management'* (3) makes no mention of SGLT2 inhibitors as part of the clinical pathway. We understand the draft CKD guideline update references SGLT2is however, the choice of a comparator on the basis of *draft* guidelines is not appropriate. Existing NICE guidelines represent the most reflective source of established and best practice comparators for finerenone. **3: How does the mechanism of action differ between SGLT2 inhibitors and finerenone, with regards to renal and cardiovascular protection?** Metabolic and haemodynamic consequences of SGLT-2i use, including glycosuria and lowering of intraglomerular pressure via activation of tubuloglomerular feedback, are the main mechanisms believed to contribute to improved kidney and CV outcomes in patients treated with SGLT-2is (4-6) In contrast, the mechanism of kidney and CV protection with finerenone involves inhibition of mineralocorticoid receptor overactivation, leading to anti-inflammatory and anti-fibrotic effects, as demonstrated in the heart and kidneys in preclinical models (7-10). This is supported by data from FIDELIO-DKD, which showed that finerenone had modest effects on systolic blood pressure and no effect on glycated haemoglobin levels throughout the duration of the study. Notably, natriuretic mechanisms may have contributed to the acute CV protection seen early on in the study (11).	

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		Feedback from clinicians has indicated that the availability of finerenone gives them another treatment modality to add to their “tool box” where for decades, they have been solely reliant on ACE inhibitors and ARBs. **4: Would a comparison between SGLT2 inhibitors and finerenone be limited by fundamental differences in the trial methodology implemented in the FIDELIO-DKD trial vs recent SGLT2 studies?** Bayer do not consider that SGLT2 inhibitors would be relevant comparators for finerenone. However, were such a comparison to occur, it would be substantially limited in its ability to compare the relative effectiveness of SGLT2 inhibitors against finerenone, as the trial methodology of recent SGLT2i studies in CKD patients utilises primary outcome measures and patient populations that are at variance with those used in the FIDELIO-DKD trial (11). Considering canagliflozin, the CREDENCE study (12) utilised a cardiorenal composite primary outcome, as opposed to the kidney-specific composite used in FIDELIO-DKD. Likewise, the proportion of trial participants in the CREDENCE study with heart failure at baseline was more than double that found in the FIDELIO-DKD study. Such differences in measures of clinical effectiveness and study population between SGLT2i studies and FIDELIO-DKD are likely to be magnified by the existing differences in the mode of action between the two therapies. (1) NICE. Guide to the methods of technology appraisal 2013. https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781 (2) IQVIA, Xponent BPI + HPA National, Counting Units, Jan-21 (3) NICE. Chronic kidney disease in adults: assessment and management. https://www.nice.org.uk/guidance/cg182 (4) Heerspink HJ, et al. Circulation 2016;134:752–772. (5) Zelniker TA, Braunwald E. J Am Coll Cardiol 2020;75:422–434.	

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		(6) Janssen. Invokana® (canagliflozin) Prescribing Information. 2020. http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/INVOKANA-pi.pdf [accessed 4 March 2020]. (7) Kolkhof P, et al. J Cardiovasc Pharmacol 2014;64:69–78. (8) Lattenist L, et al. Hypertension 2017;69:870–878. (9) Barrera-Chimal J, et al. Kidney Int 2018;93:1344–1355. (10) Grune J, et al. Hypertension 2018;71:599–608. (11) Bakris GL, et al. N Engl J Med 2020: doi: 10.1056/NEJMoa2025845. (12) Perkovic et al. N Engld J Med 2019: doi: 10.1056/NEJMoa1811744 (13) Electronic medicines compendium. Summary of product characteristics. Invokana 100mg film-coated tablets. https://www.medicines.org.uk/emc/product/8855/smpc#gref	
	Primary Care Diabetes Society	The main comparator should be established DKD management with RAS inhibition without finerenone. It would be not appropriate to compare with SGLT2 inhibitors as no head-to-head trials and SGLT2 inhibitors have well established other cardiometabolic benefits which means they will be used significantly differently from finerenone	Thank you for your comment. In order to keep the scope inclusive at this early stage, SGLT2 inhibitors have been retained. Established clinical management without finerenone, alone or in combination with angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers or direct renin inhibitors is also included as a comparator in the scope. Professional and patient organisations will have the opportunity

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			to outline their rationale to committee for the comparators it considers to be most relevant within a submission.
	Kidney Care UK	As SGLT2 inhibitors are not suitable for everyone, we believe it is important that the treatment is compared to established clinical treatment without SGLT2.	Thank you for your comment. In order to keep the scope inclusive at this early stage, SGLT2 inhibitors have been retained. Professional and patient organisations will have the opportunity to outline their rationale to committee for the comparators it considers to be most relevant within its submission.
Outcomes	Bayer	HbA1c control and diabetic ketoacidosis risk are not relevant outcomes to measure for finerenone because of its mechanism of action (1). Finerenone is not an antidiabetic agent and had no effect on mean HbA1c in the pivotal phase 3 study (FIDELIO-DKD) as evidenced by the fact that HbA1c was similar to placebo throughout (1).	Thank you for your comment. In order to keep the scope broad at this early stage, HbA1c control has been retained. Diabetic ketoacidosis, if relevant,

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		Diabetic ketoacidosis may be caused by poor control of diabetes, and has been reported in association with the use of SGLT2 inhibitors which have warnings in their SPCs (2). Diabetic ketoacidosis is not an adverse effect of interest in relation to the use of mineralocorticoid antagonists such as finerenone (1,3). (1) Bakris GL et al. N Engl J Med 2020; 383:2219-2229 DOI: 10.1056/NEJMoa2025845 (2) SPCs for canagliflozin, dapagliflozin, empagliflozin & ertugliflozin accessed in the electronic medicines compendium, March 2021 (3) Bakris GL et al. JAMA. 2015;314(9):884-894. doi:10.1001/jama.2015.10081	can be captured in the full appraisal under the broader outcome of adverse events, so has been removed.
	Primary Care Diabetes Society	Finerenone is not an anti-diabetic drug so it not appropriate to include Hba1c control as an outcome. Finerenone is not known to be associated with DKA risk so not appropriate to include this as an outcome	Thank you for your comment. In order to keep the scope broad at this early stage, HbA1c control has been retained. Diabetic ketoacidosis, if relevant, can be captured in the full appraisal under the broader outcome of adverse events, so has been removed.
	Kidney Care UK	Kidney Care UK recommends the addition of progression to RRT/ESKD, particularly due to the cost and quality of life burden of RRT/ESKD.	Thank you for your comment. Disease progression is included in the outcome list and

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			covers the outcomes of progression to renal replacement therapy (RRT) and end-stage kidney disease suggested (ESKD). Progression to RRT and ESKD have not been specified in the scope.
Economic analysis	Bayer	Bayer can confirm that the cost effectiveness of finerenone will be expressed in terms of incremental cost per quality-adjusted life year. The time horizon for estimating clinical and cost effectiveness will be lifetime. Costs will be considered from an NHS and Personal Social Services perspective.	Thank you for your comment.
	Primary Care Diabetes Society	Time horizon should be sufficient to demonstrate a reduction in the progression of DKD i.e. declining eGFR and/or demonstrate significant reduction in albuminuria AT least a 2 year time horizon would be sufficient in my opinion	Thank you for your comment.
	Kidney Care UK	The time horizon should include progression to renal replacement therapy as this is a significant cost The economic analysis should consider the increased risk of depression amongst people with CKD – the impact on HRQoL and cost of treatment (Palmer S., Vecchio M., Craig J.C. Prevalence of depression in chronic kidney disease: systematic review and meta-analysis of observational studies. Kidney Int. 2013;84:179–191.)	Thank you for your comment. The appraisal committee will consider all relevant costs and benefits when considering the cost-

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			effectiveness of this technology.
Equality	Bayer	Bayer are not aware of any equality issues affecting this appraisal at this time.	Thank you for your comment.
	Primary Care Diabetes Society	No comment	Thank you.
	Kidney Care UK	The scope should consider the difference in risk of rapid progression of CKD in different groups with protected characteristics, and consider sub-analysis of these groups. Ethnicity: (see above) Some ethnic groups, particularly Bangladeshi, appear to be more sensitive to the combined effects of proteinuria and hypertension than other ethnic groups. Age: Clinicians need to be aware that younger people with diabetes with CKD (<55 years) are at twice the risk of rapid progression than those > 65 years and thus need closer monitoring, management of risk factors and early specialist review to delay progression. We are concerned with the recommendation within the NICE CKD draft guideline (and the implications for this HTA) that 'For adults of African-Caribbean or African family origin, multiply eGFR by 41.159 if calculated using the CKD-EPI creatinine equation'. It risks exacerbating health inequalities and excluding people from those ethnic backgrounds from timely specialist assessment, diagnosis and ongoing treatment. Evidence shows that automatically increasing GFR if someone is black may be inaccurate, and can lead to overestimation of kidney function which may mean they are referred for specialised treatment late and inevitably experience poorer outcomes. There is no indication of how to apply such	Thank you for your comment. The appraisal committee will consider all relevant equality issues and make recommendations for specific groups where appropriate. This consultation is for finerenone only, and the clinical guideline updates team do not have direct access to these comments. However, on this occasion, these comments have been forwarded to the clinical

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		a formula to those of mixed race and this recommendation is not personalised or related to muscle mass. The historic formula is based on an unrepresentative group of African Americans and should not be used to determine access to specialised treatment for adults in the UK in 2021. We note that the US National Kidney Federation and American Society of Nephrology Taskforce has started work to address this problem and "Ensure that GFR estimation equations provide an unbiased assessment of kidney function so that patients, clinicians, laboratories, and public health officials can make informed decisions to ensure equity and personalized care for patients with kidney diseases." We think that this approach should apply in the UK and urge NICE to reconsider the perpetuation of this outdated approach. With regard to this HTA of Finererone, people of African or African-Caribbean family origin may be excluded from timely treatment with Finerenone if the draft recommendation regarding eGFR multiplication is adopted.	guideline updates team for consideration. Where appropriate, the committee will consider any relevant recommendations made in the final NICE guideline on chronic kidney disease when considering the recommendations for this appraisal.
Other considerations	Bayer	Bayer have no additional considerations to suggest.	Thank you for your comment.
	Primary Care Diabetes Society	No comment	Thank you.
Innovation	Bayer	As described below, the technology is innovative in having a completely novel mode of action which differs from all existing and emerging new treatment options for CKD in T2D. This mode of action is based on an understanding of the role of inflammation and fibrosis in the pathophysiology of CKD in T2D. As evidence of the success of this approach, clinically significant renal and CV benefits have been demonstrated in patients with CKD and T2D already on background guideline-directed therapy, plus well-controlled glycated haemoglobin and blood pressure levels (1,2).	Thank you for your comment. The innovative nature of this technology will be considered by the committee. No changes have been made to the scope.

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		The magnitude of the benefits observed clearly represent a step-change in reducing the risk of CKD progression and adverse CV events in patients with CKD and T2D (1,2). It has been over two decades since there have been any new pharmacological treatment options to delay the progression of CKD in T2D. Over this period, the focus has primarily been on improved management of hyperglycemia and hypertension, with the use of ACEis or ARBs (3). Recently, SGLT2is, in addition to an ACEi or ARB, have demonstrated delayed progression of CKD in T2D (3). However, while optimizing therapy with RAS blockers and SGLT2 inhibitors has slowed CKD progression, it has not fully stopped it (3). Understanding of the drivers of CKD progression has also evolved, with growing evidence that pathophysiological overactivation of the mineralocorticoid receptor (MR) leads to inflammation and fibrosis in the kidneys. Therefore, blockade of the MR represents a completely novel treatment approach to slow CKD progression in T2D (3). Finerenone is a novel, nonsteroidal, selective MR antagonist that has a high affinity for the MR and a unique binding mode that has been shown to reduce inflammation and fibrosis in animal models (3). In the pivotal phase 3 study (FIDELIO-DKD) in patients with CKD and T2D, the benefits of finerenone were clinically significant and were obtained on a background of guideline-directed therapy, including RAS blockade at a maximum labeled dose, plus well-controlled glycated haemoglobin and blood pressure levels (1).	

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		(1) Bakris GL et al. N Engl J Med 2020; 383:2219-2229 DOI: 10.1056/NEJMoa2025845 (2) Filippatos G et al. *Circulation.* 2021;143:540–552 DOI: 10.1161/CIRCULATIONAHA.120.051898 (3) Agarwal R et al. Nephrol Diab Transplant (2020) 1-10 doi: 10.1093/ndt/gfaa294	
	Primary Care Diabetes Society	Finerenone is a novel therapy for DKD with potential to have additive benefits to current standard of care including RAS inhibition. I would consider this a step-change in the management of DKD but once again I feel finerenone should be considered an additional pillar of DKD management	Thank you for your comment. The innovative nature of this technology will be considered by the committee. No changes have been made to the scope.
	Kidney Care UK	We do consider the treatment to be innovative and it has potential to make a significant and substantial impact on health-related benefits.	Thank you for your comment. The innovative nature of this technology will be considered by the committee. No changes have been made to the scope.
Questions for consultation	Bayer	1. *Have all relevant comparators for finerenone been included in the scope?* Bayer do not consider that SGLT2i should be listed as comparators – see response to question 2. For decades, there have been no treatment options for	Thank you for your comment. In order to keep the scope inclusive at this

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		CKD apart from ACEi and ARB for retarding the progression toward end-stage renal disease. Bayer consider the comparator to finerenone to be standard of care established in clinical practice which is ACEi/ARB. Finerenone is an add-on therapy to ACEi/ARB addressing residual risk of renal and CV outcomes and CKD disease progression (see response to question 3). 2. *Is it appropriate to include SGLT2 inhibitors as comparators? If so, should it be limited to any specific SGLT2 inhibitors?* Bayer do not consider that SGLT2i should be listed as comparators. Please refer to Bayer's response above regarding the section – 'Comparators'. 3. *Is it anticipated that finerenone would be given in addition to an ACE inhibitor or an ARB?* Yes, finerenone will be given in addition to an ACE inhibitor or an ARB. In the FIDELIO trial, finerenone was given on top of ACE inhibitor/ ARB. 4. *Which treatments are considered to be established clinical practice in the NHS for chronic kidney disease in people with type 2 diabetes? Which treatments would finerenone be likely to displace in this population?* For decades, there have been no treatment options for CKD apart from ACEi and ARB for retarding the progression toward end-stage renal disease. Bayer consider ACEi/ARBs to be established clinical practice in this indication. Finerenone would be used in add-on to ACEi/ARB to reduce the residual risk of CV and renal events and would not displace any treatment. 5. *Are the outcomes listed appropriate?*	early stage, SGLT2 inhibitors have been retained. The comparators also include established clinical management without finerenone, alone or in combination with angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers or direct renin inhibitors. In response to the outcomes suggested as inappropriate, diabetic ketoacidosis risk has been removed from the outcomes listed in the scope. However, in order to keep the scope broad at this early stage, HbA1c control has been retained. The innovative nature of this technology will be considered by the committee. No changes relating to innovation

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		Bayer do not consider that all suggested outcomes are appropriate. Please refer to Bayer's response above regarding the section – 'Outcomes'. 6. *Are there any subgroups of people in whom finerenone is expected to be more clinically effective and cost effective or other groups that should be examined separately?* Bayer are not aware at this time of any subgroups that may be more clinically and cost effective or of any other groups that should be examined separately. 7. *Where do you consider finerenone will fit into the existing NICE pathway, chronic kidney disease?* Finerenone will be considered as an add-on therapy to ACEi/ARB to further reduce the risk of CKD progression and adverse CV and renal outcomes. 8. *Do you consider finerenone to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?* Bayer consider that finerenone is an innovative medicine and offers a new treatment option for clinicians and patients in a field of medicine where there have been no new specific treatment options for decades. Please refer to Bayer's response above regarding the section – 'Innovation'.	have been made to the scope.

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		9. *Do you consider that the use of finerenone can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?* Bayer are not aware at this time of any benefits that are unlikely to be captured in the QALY calculation. 10. *Do you consider that there will be any barriers to adoption of this technology into practice?* Bayer are not aware at this time of any potential barriers to adoption of finerenone into practice.	
	Primary Care Diabetes Society	I anticipate finerenone would be given in addition to RAS inhibition which is current standard of care. Finerenone would not displace any current treatments but could be considered as add-on therapy to RAS inhibitors and also add-on to SGLT2 inhibitors or instead of SGLT2 inhibitors if they are not tolerated or contraindicated. (FIDELIO-DKD allowed SGLT2 inhibitor treatment in around 5% of trial participants)	Thank you for your comment. The comparators in the scope include established clinical management without finerenone, alone or in combination with angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers or direct renin inhibitors.
	Kidney Care UK	**Where do you consider finerenone will fit into the existing NICE pathway, chronic kidney disease?** We consider that Finerenone would	Thank you for your comment. These have

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		fit in the NICE CKD pathway after 'establishing cause'. If diabetes is considered to be the cause then treatment with Finererone should be considered. **Barriers to treatment:** the major barrier to treatment is the current low rate of implementation of the NICE recommended kidney function tests in people with diabetes (Only 54% of people with diabetes are having the NICE recommended regular GP-based urine tests that can enable early identification of kidney disease (HQIP (2017) National Chronic Kidney Disease Audit, London) The removal of ACR testing from QOF in 2014 is likely to have contributed to the lower number of patients having an annual screen for ACR. Failing to undertake these tests is likely to reduce the identification of people who will benefit from the use of finerenone In addition, there is evidence of significant problems with coding of CKD in primary care (eg >50% of CKD was uncoded, Molokhia M et al, British Journal of General Practice 2020; 70 (700): e785-e792) meaning there are likely to be many people with CKD who are excluded from treatment because they are not identified or recorded.	been noted. No changes have been made to the scope.
Any additional comments on the draft scope	Bayer	Bayer have no further comments on the draft scope and consider that appraisal through the STA process is appropriate.	Thank you for your comment.
	Kidney Care UK	Kidney Care UK believes it's vital that people are provided with lifestyle and diet advice so they can take action to reduce their risk of further kidney damage, and it is important that any NICE guidance resulting from this review recommends the provision of suitable advice	Thank you for your comment. Where appropriate, the committee will reference relevant NICE guidance on lifestyle

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			and diet advice for people with chronic kidney disease.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

InDependent Diabetes Trust