

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Canagliflozin for treating diabetic kidney disease in adults with type 2 diabetes [ID1653]

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of canagliflozin within its marketing authorisation for treating diabetic kidney disease in adults with type 2 diabetes.

Background

Chronic kidney disease (CKD) is a condition where the kidneys do not work as well as they should and it is linked with adverse outcomes including cardiovascular disease⁴. It is common, in people who have diabetes, in which it is known as diabetic kidney disease. This is because people with diabetes have too much glucose in their blood and this can damage the tiny filters in the kidneys¹. People with CKD do not usually have symptoms during the early stages of the disease but symptoms including weight loss and poor appetite, swollen ankles, feet or hands, shortness of breath, tiredness, feeling sick and itchy skin can develop as the disease progresses¹. The severity of CKD is determined by the estimated glomerular filtration rate (eGFR) of which there are 6 categories (normal, mild reduction, mild to moderate reduction, moderate to severe reduction, severe reduction and kidney failure) and albumin to creatinine ratio (ACR) with 3 categories (normal to mild increase, moderate increase and severe increase).¹ An ACR of more than 3 mg/mmol is an indicator for albuminuria, when albumin, a protein that is normally found in the blood, is found in the urine. CKD can progress to end-stage kidney disease (ESKD) in a small but significant percentage of people.

Approximately 2.9 million people are currently diagnosed with type 2 diabetes in England.^{2,3} Around 20% of people with diabetes will need treatment for kidney disease during their lifetime³ and at least 10,350 people in the UK have end stage kidney failure caused by diabetes³. More than 1 in 3 people who need kidney dialysis or a transplant have diabetes³. For people with diabetes having renal replacement treatment, survival rates are lower compared with those without diabetes⁵.

For people with CKD and diabetes NICE clinical guideline 182 '[chronic kidney disease in adults: assessment and management](#)' recommends:

- keeping systolic blood pressure below 130 mmHg (target range 120–129 mmHg) and the diastolic blood pressure below 80 mmHg
- a drug that blocks or inhibits the renin-angiotensin system including angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs) and direct renin inhibitors to manage blood pressure if there is an ACR of 3 mg/mmol or more.

People with ESKD may require dialysis or a kidney transplant¹.

The technology

Canagliflozin (Invokana, Napp Pharmaceuticals Ltd) is a selective sodium glucose-cotransporter 2 (SGLT-2) inhibitor. It lowers blood glucose in people with type 2 diabetes by blocking the reabsorption of glucose in the kidneys and promotes excretion of excess glucose in the urine. It also acts on the renal mechanism that leads to a feedback signal that causes afferent arteriolar vasoconstriction, an acute fall in glomerular perfusion and pressure, as well as diminished extracellular plasma volume and blood pressure. Canagliflozin is administered orally.

Canagliflozin does not currently have a marketing authorisation in the UK for treating diabetic kidney disease in people with type 2 diabetes. It has been studied in clinical trials as an adjuvant treatment to standard of care compared with placebo with standard of care in adults aged 30 years or older with type 2 diabetes. One trial included people with type 2 diabetes mellitus, stage 2 or 3 chronic kidney disease and macroalbuminuria.

Canagliflozin has a UK marketing authorisation for treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise:

- as monotherapy when metformin is considered inappropriate due to intolerance or contraindications
- in addition to other medicinal products for the treatment of diabetes.

Intervention(s)	Canagliflozin
Population(s)	Adults with type 2 diabetes and diabetic kidney disease with albuminuria
Comparators	Established clinical management without canagliflozin
Outcomes	The outcome measures to be considered include: <ul style="list-style-type: none">• morbidity including cardiovascular outcomes, disease progression (such as renal replacement, ESKD) and markers of disease progression (such as serum creatinine, albuminuria)• HbA1c control• diabetic ketoacidosis risk• mortality• adverse effects of treatment• health-related quality of life.

Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
Other considerations	<p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>Canagliflozin in combination therapy for treating type 2 diabetes (2014). NICE technology appraisal guidance 315</p> <p>Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes (2016). NICE technology appraisal guidance 390</p> <p>Related Guidelines:</p> <p>Renal replacement therapy and conservative management (2018). NICE guideline 107</p> <p>Chronic kidney disease in adults: assessment and management (2014, updated 2015). NICE clinical guideline 182</p> <p>Type 2 diabetes in adults: management (2015, updated 2019). NICE guideline 28</p> <p>Chronic kidney disease: managing anaemia (2015). NICE guideline 8</p> <p>Guidelines in development</p> <p>Chronic kidney disease: assessment and management (update) NICE guideline. Publication expected July 2020</p> <p>Related Quality Standards:</p> <p>Chronic kidney disease in adults (2011, updated 2017). NICE quality standard 5</p> <p>Renal replacement therapy services for adults (2014, updated 2018). NICE quality standard 72</p> <p>Diabetes in adults (2011, updated 2016) NICE quality standard 6</p> <p>Related NICE Pathways:</p> <p>Chronic kidney disease (last updated 2019). NICE pathway</p>

Related National Policy	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 15 'Adult specialists renal services' page 65.</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2.</p>
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References

- 1 NHS choices (2019) [Chronic kidney disease](#). Accessed September 2019.
- 2 Diabetes UK (2018) [Diabetes prevalence](#). Accessed September 2019.
- 3 Diabetes UK (2019) [Us, diabetes and a lot of facts and stats](#). Accessed September 2019.
- 4 Levey et al (2005) Kidney Disease: Improving Global Outcomes (KDIGO). Kidney International, 67 2089-2100. Accessed December 2019. Available from: <https://kdigo.org/wp-content/uploads/2017/01/Position-Paper-Definition-and-Classification-of-Chronic-Kidney-Disease-in-Adults-Worldwide-2004.pdf>
- 5 Shaw C, et al (2012). Chapter 2 - UK RRT Adult Prevalence in 2011- national and centre-specific analyses. Accessed December 2019. Available from: <https://www.renalreg.org/wp-content/uploads/2014/09/Report2012.pdf>.