NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

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

Draft scope (pre-referral)

Draft remit/appraisal objective

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

Background

Chronic kidney disease (CKD) is a condition where the kidneys do not work as well as they should. It is common, in people who have diabetes. This is because people with diabetes have too much glucose in their blood and this can damage the tiny filters in the kidneys[1]. 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 progresses[1]. The severity of CKD is determined by the estimated glomerular filtration rate (eGFR) of which there are 6 stages and albumin to creatine ratio (ACR) with 3 stages. For both eGFR and ACR, a higher stage indicates more severe kidney disease[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 lifetime[3] and at least 10,350 people in the UK have end stage kidney failure caused by diabetes[3]. More than 1 in 3 people who need kidney dialysis or a transplant have diabetes[3].

NICE clinical guideline 182 'chronic kidney disease in adults: assessment and management' recommends offering people with CKD and diabetes and an ACR of 3 mg/mmol or more a drug that blocks or inhibits the renin-angiotensin-aldosterone system including angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), direct renin inhibitors and aldosterone antagonists. People with ESKD may require dialysis or a kidney transplant[1].

The technology

Canagliflozin (Invokana, Janssen-Cilag, UK commercialisation by 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 chronic 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 chronic kidney disease and type 2 diabetes
Comparators	Established clinical management without canagliflozin
Outcomes	The outcome measures to be considered include: • incidence of kidney disease • doubling of serum creatinine • progression of albuminuria • renal mortality • HbA1c control • diabetic ketoacidosis risk • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. 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. Costs will be considered from an NHS and Personal Social Services perspective.

Other considerations	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.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** Canagliflozin in combination therapy for treating type 2 diabetes (2014). NICE technology appraisal guidance 315 Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes (2016). NICE technology appraisal guidance 390 **Related Guidelines:** Renal replacement therapy and conservative management (2018). NICE guideline 107 Chronic kidney disease in adults: assessment and management (2014, updated 2015). NICE clinical guideline 182 Type 2 diabetes in adults: management (2015, updated 2019). NICE guideline 28 Chronic kidney disease: managing anaemia (2015). NICE guideline 8 **Guidelines in development** Chronic kidney disease: assessment and management (update) NICE guideline. Publication expected July 2020 **Related Quality Standards:** Chronic kidney disease in adults (2011, updated 2017). NICE quality standard 5 Renal replacement therapy services for adults (2014, updated 2018). NICE quality standard 72 Diabetes in adults (2011, updated 2016) NICE quality standard 6 **Related NICE Pathways:** Chronic kidney disease (last updated 2019). NICE pathway
Related National	The NHS Long Term Plan, 2019. NHS Long Term Plan

Policy	NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 15 'Adult specialists renal services' page 65. Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2.

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for chronic kidney disease with type 2 diabetes?

Can the population defined in this scope already have treatment with canagliflozin based on recommendations in TA315 and TA390? If there are patients in this scope population who cannot currently have treatment with canagliflozin, please outline this population and how they can be identified in clinical practice.

Are the outcomes listed appropriate?

Are there any subgroups of people in whom canagliflozin is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider canagliflozin will fit into the existing NICE pathway, Chronic kidney disease?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which canagliflozin will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider canagliflozin 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)?

Do you consider that the use of canagliflozin can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the process of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/process-guide-addendum-fast-track.pdf), which states the process to be used where a fast track appraisal case is made. Is canagliflozin suitable for the fast track appraisal process?

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.

