Appendix G - professional organisation statement template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Canagliflozin in combination therapy for treating type 2 diabetes

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: [redacted]

Name of your organisation: Association of British Clinical Diabetologists (ABCD) and Royal College of Physicians (RCP).

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology?
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc)?
- other? (please specify)

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What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice?
Type 2 diabetes is common, affecting 5-7% of the adult population with a projected prevalence of 10% by 2020. The vast majority of cases are managed within primary care. Recent National Diabetes Audit shows significant geographical variation in care processes and outcomes. There is a clear evidence base demonstrating that early effective control of blood glucose can reduce the development and progression of microvascular (and potentially macrovascular) complications.

Are there differences of opinion between professionals as to what current practice should be?
The algorithm for placement of different therapies in Type 2 diabetes is consensus rather than evidence based . Although the American Diabetes Association and the European Association for the Study of Diabetes have produced broad guidance to help selection of therapy for diabetes , this is not totally aligned with the current (although under revision) NICE guidelines for type 2 diabetes . The early use of injectable (insulin and GLP-1 analogue) therapy and the relative risks of weight gain and hypoglycaemia versus the established evidence base for the beneficial impact of glycaemic control with older sulfonylurea agents remains an area of contention amongst opinion leaders in diabetes .

What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?
In terms of the oral therapies available for the treatment of type 2 diabetes, there, there are a number of other therapeutic agents.
Metformin therapy is the accepted first line of treatment. It has a good safety record and has been shown to have several beneficial properties. It acts by improving insulin sensitivity although the mechanism is not totally clear. As monotherapy it may not be sufficient to treat T2DM to target. There is a significant proportion of individuals who are intolerant, usually GI disturbance. It is contraindicated in renal impairment.
Sulphonyl ureas stimulate insulin secretion at a distal point in the pathway. They have a good safety record but there is a serious risk of hypoglycaemia as the glucose sensing mechanisms are overridden. There is ongoing debate on their effect on cardiac remodelling.
Pioglitazone acts through improvement of insulin sensitivity, acting on a nuclear receptor. Rosiglitazone in the same class was withdrawn due to questions over cardiovascular safety and troglitazone withdrawn due to liver toxicity. None of these applies to pioglitazone although it has been found to cause peripheral osteoporosis and to increase the risk of bladder cancer. Due to fluid accumulation there is a risk of cardiac failure and there is considerable weight gain. Due to the above, use is declining.
Acarbose as a glucose absorption inhibitor is mild and little used in the UK.

The DPPIV inhibitors are relatively new to the market and clinical experience is limited. They effectively lower blood glucose but there are questions surrounding their longer term safety and particularly the risk of pancreatitis.

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?
Patients with a family history of diabetes with adverse outcomes, those with the 'full house' of features of metabolic syndrome , renal disease (assessed by albuminuria and eGFR) , smokers , early onset T2, consistent poor control all carry a worse prognosis

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?
Ultimately this therapy will be used in primary care, although early clinical experience is likely to be through specialist recommendation.

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?
Not curently licensed in the UK.

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.
NICE –Type 2 – under review
ADA-EASD best practice guidelines for T2DM 2012

The advantages and disadvantages of the technology. NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?
The advantage of this class of agent is that they work through a different mechanism when compared to the other oral agents currently available. There is potential, therefore, that the SGLT2 inhibitors, including canagliflozin, will be a useful adjunct to other first line therapies or in addition to insulin treatment. The fact that the treatment is orally effective in a common condition is likely to lead to widespread use. Clinical trials suggest a slightly higher rate of side effects associated with this class compared with alternatives, but clinical experince will be a deciding factor. The reported weight loss with canagliflozin treatment is valuable given that T2DM is associated with weight gain and insulin, glitazones and SU therapy exacerbate this.

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.
The standard rules surrounding postmarketing surveillance and adverse event reporting will apply.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?
The clinical trials have largely focussed on individuals with type 2 diabetes who have levels of glycaemic control which are only slightly over target. While this is the appropriate target group, it is highly likely that individuals with considerably higher glycaemic indices will receive this treatment in routine clinical practice. Outcomes in these individuals have not been thoroughly explored.
The trials use the usual surrogate markers of response in diabetes, namely measurement of blood glucose and HbA1c. Lipid parameters have been measured and a rise in LDL cholesterol noted. In this context, cardiovascular outcomes will need to be closely monitored in longer term studies.

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?
In view of the mode of action of this agent and class, side effects focus on osmotic symptoms and risk of bladder and mycotic infection. These may severely impact on quality of life, but ongoing clinical experience is required. Trial data to date are encouraging in this regard suggesting relatively low level side effects and good tolerability.

Any additional sources of evidence
Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.
Data accumulation is ongoing. See the abstract data from ADA and EASD (and IDF later in 2013).

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Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

Other than prescribing costs, there should be no associated increase in budgetary requirement.

Equality
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 this appraisal:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/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 lead to recommendations that 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.
No issues identified