NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Dapagliflozin and empagliflozin, in combination with insulin, for treating type 1 diabetes

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dapagliflozin and empagliflozin within their marketing authorisation for treating type 1 diabetes.

Background

Type 1 diabetes results from destruction of the cells that normally make insulin. Loss of insulin secretion results in high blood glucose and other metabolic and haematological abnormalities, which have both short-term and long-term adverse effects on health. Over years, type 1 diabetes causes tissue damage which, if not detected and managed early, can result in disability: blindness, kidney failure and foot ulceration leading to amputation, as well as premature heart disease, stroke and death. The risk of all of these complications is greatly reduced by treatment that keeps circulating glucose levels to as near normal as possible, reducing tissue damage.

Approximately 3.8 million adults in England have diabetes, and around 10% of diabetes cases are type 1[1].

Type 1 diabetes is treated by insulin replacement, supported by active management of other cardiovascular risk factors, such as hypertension and high circulating lipids. Insulin replacement therapy aims to recreate normal fluctuations in circulating insulin concentrations. Flexible insulin therapy usually involves self-injecting multiple daily doses of insulin, with doses adjusted based on exercise, food intake and other factors, including current blood glucose. NICE has issued recommendations on insulin therapy in NICE guideline 17. The guideline also recommends consideration of adding metformin to insulin therapy in some circumstances.

The technologies

Dapagliflozin (Forxiga, AstraZeneca) and empagliflozin (Jardiance, Boehringer Ingelheim and Eli Lilly) are selective sodium-glucose co-transporter 2 (SGLT-2) inhibitors. They block the reabsorption of glucose in the kidneys and promote excretion of excess glucose in the urine. They are administered orally.

Dapagliflozin and empagliflozin do not currently have marketing authorisations in the UK for treating type 1 diabetes. Dapagliflozin and empagliflozin are being studied in combination with insulin in placebo controlled trials for adults with type 1 diabetes that is inadequately controlled on insulin monotherapy.

Dapagliflozin and empagliflozin have marketing authorisations for treating type 2 diabetes as an adjunct to diet and exercise as combination therapy or as monotherapy when metformin is not tolerated.

Intervention(s)	• Dapagliflozin in combination with insulin • Empagliflozin in combination with insulin
Population(s)	Adults with type 1 diabetes that is inadequately controlled on insulin monotherapy
Comparators	Insulin monotherapy
Outcomes	The outcome measures to be considered include: • mortality • complications of diabetes, including cardiovascular, renal and eye • HbA1c/glycaemic control • body mass index • frequency and severity of hypoglycaemia • changes in cardiovascular risk factors • total daily insulin dose • adverse effects of treatment, including urinary tract infections, genital infections and malignancies • 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, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes (2016). NICE technology appraisal 390. Review date May 2019. Dapagliflozin in triple therapy for treating type 2 diabetes (2016) NICE technology appraisal 418. Review date November 2019. Dapagliflozin in combination therapy for treating type 2 diabetes (2013) NICE technology appraisal 288. Review date May 2017. Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (2008) NICE technology appraisal 151. Review date: on static list. Appraisals in development (including suspended appraisals) Diabetes - buccal insulin. NICE technology appraisal guidance [ID311]. Suspended. Related Guidelines: Type 1 diabetes in adults: diagnosis and management (2015). NICE guideline 17. To be scheduled. Related Interventional Procedures: Allogeneic pancreatic islet cell transplantation for type 1 diabetes mellitus (2008). NICE interventional procedures guidance 257. Related Quality Standards: Diabetes in adults (2016). NICE quality standard 6. Related NICE Pathways: Type 1 diabetes in adults (2016) NICE pathway.
Related National Policy	NHS England. Manual for prescribed specialised services 2016/17. Chapter 68. Islet transplantation service (adults) Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1 and 2.

	https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Is the population defined appropriately? Would dapagliflozin and empagliflozin, in combination with insulin, be used only in adults with type 1 diabetes mellitus that is inadequately controlled on insulin monotherapy?

Have all relevant comparators for dapagliflozin and empagliflozin, in combination with insulin, been included in the scope? Which treatments are considered to be established clinical practice in the NHS for type 1 diabetes that is inadequately controlled on insulin monotherapy? Is metformin in combination with insulin a relevant comparator?

Are the outcomes listed appropriate?

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

Where do you consider dapagliflozin and empagliflozin will fit into the existing NICE pathway, Type 1 diabetes in adults?

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 dapagliflozin and empagliflozin 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 dapagliflozin and empagliflozin to be innovative in there 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 dapagliflozin and empagliflozin 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 Multiple Technology Appraisal (MTA) 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).

References

1 Public Health England. "3.8 million people in England now have diabetes." Available at https://www.gov.uk/government/news/38-million-people-in-england-now-have-diabetes. Accessed June 2017.