NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Dulaglutide for treating type 2 diabetes

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dulaglutide within its marketing authorisation for treating type 2 diabetes.

Background

Diabetes mellitus is a chronic metabolic disorder characterised by elevated blood glucose levels (hyperglycaemia) resulting from a lack of the hormone insulin or resistance to its action. Type 2 diabetes results from reduced insulin secretion or reduced tissue sensitivity to insulin (known as insulin resistance). If not managed effectively, diabetes mellitus can lead to kidney failure, blindness, limb amputation, and damage to the nervous system, peripheral vasculature and skin. Cardiovascular disease is the most common complication of type 2 diabetes and is the greatest cause of morbidity and premature death. Life expectancy is reduced by up to 10 years in people with diabetes.

There were over 3.1 million people in England with diagnosed diabetes mellitus in 2017.[1] However, many people with type 2 diabetes are undiagnosed, and so the number of people with the condition may be higher than reported. The UK prevalence of type 2 diabetes is rising because of increased prevalence of obesity, decreased physical activity and increased life expectancy after diagnosis because of better cardiovascular risk protection. Type 2 diabetes is particularly prevalent in people of African, South Asian and Caribbean family origin.

NICE guideline 28 '[type 2 diabetes in adults: management]' recommends reinforcing advice on diet, lifestyle and adherence to drug treatment for all people with type 2 diabetes. If there is inadequate glycaemic control on diet and exercise alone:

- NG28 recommends standard release metformin. When metformin is contraindicated or not tolerated a dipeptidyl peptidase-4 (DPP-4) inhibitor, pioglitazone or a sulfonylurea is recommended.

- NICE [technology appraisal 390] recommends the selective sodium glucose-cotransporter 2 (SGLT-2) inhibitors canagliflozin, dapagliflozin and empagliflozin as options for monotherapy in adults for whom metformin is contraindicated or not tolerated and when diet and exercise alone do not provide adequate glycaemic control, only if a DPP‑4 inhibitor would

otherwise be prescribed and a sulfonylurea or pioglitazone is not appropriate.

When there is inadequate glycaemic control following initial therapy, treatment is intensified:

- NICE guideline 28 recommends dual therapy with metformin plus a DPP-4, pioglitazone or a sulfonylurea. When metformin is contraindicated or not tolerated alternative dual therapies such as a DPP-4 and pioglitazone, a DPP-4 and a sulfonylurea or pioglitazone and a sulfonylurea are recommended.

- NICE technology appraisals 315, 288 and 336 recommend a SGLT-2 inhibitor (canagliflozin, dapagliflozin and empagliflozin respectively) in a dual therapy regimen with metformin, only if a sulfonylurea is contraindicated or not tolerated or the person is at significant risk of hypoglycaemia or its consequences.

If there is inadequate glycaemic control following first intensification, treatment is intensified further:

- NICE guideline 28 recommends triple therapy with metformin (this includes metformin plus a sulfonylurea plus either a DPP-4 inhibitor or pioglitazone) or insulin based treatment. A glucagon-like peptide-1 (GLP-1) mimetic can be combined with metformin and sulfonylurea for specific subgroups if triple therapy is not effective, not tolerated or is contraindicated.

- NICE technology appraisal 418 recommends that triple therapy with dapagliflozin is a treatment option only in combination with metformin and a sulfonylurea. NICE technology appraisals 315 and 336 recommend that triple therapy with canagliflozin or empagliflozin are options in combination with either metformin plus a sulfonylurea or metformin plus a thiazolidinedione (pioglitazone). Canagliflozin, dapagliflozin and empagliflozin are also recommended as treatment options with insulin with or without other antidiabetic drugs.

The technology

Dulaglutide (Trulicity; Eli Lilly) is a GLP-1 mimetic. It works by stimulating the body's natural production of insulin thereby helping to reduce blood glucose levels. It is administered subcutaneously.

Dulaglutide has a marketing authorisation in the UK for treating adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control:

- as monotherapy, when diet and exercise alone do not provide adequate glycaemic control in patients for whom the use of metformin is considered inappropriate due to intolerance or contraindications.

- as add-on therapy in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

Intervention(s)	Dulaglutide alone or with other antidiabetic agents
Population(s)	Dulaglutide monotherapy: • Adults with type 2 diabetes that is inadequately controlled with diet and exercise alone and for whom the use of metformin is considered inappropriate due to intolerance or contraindications Dulaglutide with other antidiabetic agents: • Adults with type 2 diabetes that is inadequately controlled with one or more anti-diabetic agents
Comparators	The following interventions as monotherapy: • sulfonylureas • pioglitazone • DPP-4 inhibitors • SGLT-2 inhibitors (if a DPP-4 inhibitor would otherwise be prescribed and a sulfonylurea or pioglitazone is not appropriate) The following interventions in combination regimens: • sulfonylureas • DPP-4 inhibitors • pioglitazone • SGLT-2 inhibitors • other GLP-1 mimetics • insulin

Outcomes	The outcome measures to be considered include: • mortality • complications of diabetes, including cardiovascular, renal and eye • HbA1c/glycaemic control • change in body weight • body Mass Index • frequency and severity of hypoglycaemia • changes in cardiovascular risk factors • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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:** 'Dapagliflozin in triple therapy for treating type 2 diabetes' (2016) NICE Technology Appraisal 418. Review date November 2019. 'Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes' (2016) NICE Technology Appraisal 390. Review date May 2019. 'Empagliflozin in combination therapy for treating type 2

	diabetes' (2015) NICE Technology Appraisal 336.Evidence was reviewed in March 2018. 'Canagliflozin in combination therapy for treating type 2 diabetes' (2014). NICE Technology Appraisal 315. Evidence was reviewed in October 2017. 'Dapagliflozin in combination therapy for treating type 2 diabetes' (2013). NICE Technology Appraisal 288. Evidence was reviewed in July 2015 and the guidance partially updated in TA418. **Appraisals in development:** Ertugliflozin as monotherapy and in dual therapy for treating type 2 diabetes. NICE technology appraisals guidance [ID1158]. Publication expected: TBC. Ertugliflozin in a triple therapy regimen for treating type 2 diabetes. NICE technology appraisals guidance [ID1160]. Publication expected: TBC. **Related Guidelines:** 'Type 2 diabetes in adults: management' (2015, updated 2017) NICE guideline NG28. Review date: 2020. **Related Quality Standards:** Quality Standard No. 6, Mar 2011, updated 2016 'Diabetes in adults'. **Related NICE Pathways:** NICE Pathway: Diabetes, Pathway created: May 2011: https://pathways.nice.org.uk/pathways/diabetes.
Related National Policy	NHS England Manual for Prescribed Specialised Services 'Adult specialist endocrinology services' (chapter 9) https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf 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

Have all relevant comparators for dulaglutide been included in the scope?

Are the outcomes listed appropriate?

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

Where do you consider dulaglutide will fit into the existing NICE pathway for diabetes, https://pathways.nice.org.uk/pathways/diabetes?

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 duglalutide is 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 dulaglutide 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 dulaglutide 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 methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Diabetes UK Diabetes Prevalence 2017. Accessed June 2018