NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Tirzepatide for treating type 2 diabetes

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of tirzepatide 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)[1]. If not managed effectively, diabetes mellitus can lead to kidney failure, blindness, foot problems, and damage to the nervous system[2]. People with diabetes are also more at risk of cardiovascular disease[3].

There were 3.3 million people in England with diagnosed diabetes mellitus in 2019, of which around 90% had type 2 diabetes[4]. However, an estimated 1 million further people have undiagnosed type 2 diabetes in the UK[4]. The UK prevalence of type 2 diabetes is rising, which has been linked to an increasing prevalence of obesity[5]. People from Black African, African Caribbean and South Asian family backgrounds are at a higher risk of developing type 2 diabetes from a younger age[6].

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 blood glucose levels are not controlled by diet and exercise alone:

- NICE guideline 28 recommends first-line drug treatment with standard release metformin. For people with chronic heart failure, cardiovascular disease or at high risk of cardiovascular disease, it recommends considering a selective sodium glucose-cotransporter 2 (SGLT2) inhibitor in addition to metformin.

- When metformin is contraindicated or not tolerated a dipeptidyl peptidase-4 (DPP-4) inhibitor, pioglitazone or a sulfonylurea is recommended. For people with chronic heart failure, cardiovascular disease or at high risk of cardiovascular disease, or for people who meet the criteria in NICE technology appraisal guidance 390, or TA572, an SGLT2 inhibitor is recommended.

When there is inadequate glycaemic control following first-line treatment, treatment is intensified:

- NICE guideline 28 recommends adding a DPP-4 inhibitor, pioglitazone or a sulfonylurea, or an SGLT2 inhibitor for people who meet the criteria in NICE technology appraisal guidance 315, TA572, TA288, or TA336.

If there is inadequate glycaemic control with dual therapy, treatment is intensified further:

- NICE guideline 28 recommends triple therapy by adding a DPP-4 inhibitor, pioglitazone or a sulfonylurea, or an SGLT2 inhibitor for people who meet the criteria in NICE technology appraisal guidance 315, TA418, TA336, or TA583, or starting insulin-based treatment.

- If metformin is contraindicated or not tolerated, NICE guideline 28 recommends insulin-based treatment.

- If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, NICE guideline 28 recommends switching one drug for a glucagon-like peptide-1 (GLP-1) mimetic for some groups of people.

The technology

Tirzepatide (brand name unknown, Eli Lilly) is a dual receptor agonist that acts at the receptors of both the GIP and GLP-1 hormones. These hormones act to stimulate insulin secretion. It is administered by subcutaneous injection.

Tirzepatide does not currently have a marketing authorisation in the UK for treating type 2 diabetes. It has been studied in clinical trials in people with type 2 diabetes alone or in combination with other antidiabetic agents.

Intervention(s)	Tirzepatide alone or with other antidiabetic agents
Population(s)	Tirzepatide monotherapy: • Adults with type 2 diabetes that is inadequately controlled with diet and exercise alone and in whom the use of metformin is considered inappropriate due to intolerance Tirzepatide with other antidiabetic agents: • Adults with type 2 diabetes that is inadequately controlled with one or more antidiabetic agents

Comparators	The following interventions as monotherapy: • sulfonylureas • pioglitazone • DPP-4 inhibitors • SGLT-2 inhibitors (for people with chronic heart failure, cardiovascular disease or at high risk of cardiovascular disease, or if a DPP-4 inhibitor would otherwise be prescribed and a sulfonylurea or pioglitazone is not appropriate) • insulin The following interventions in combination regimens: • sulfonylureas • DPP-4 inhibitors • pioglitazone • GLP-1 mimetics • SGLT-2 inhibitors • insulin
Outcomes	The outcome measures to be considered include: • HbA1c/glycaemic control • complications of diabetes, including cardiovascular, renal and eye • mortality • 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. The availability and cost of biosimilar and generic products should be taken into account.
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:** Ertugliflozin with metformin and a dipeptidyl peptidase-4 inhibitor for treating type 2 diabetes (2019) NICE technology appraisal guidance 583. Review date 2022. Ertugliflozin as monotherapy or with metformin for treating type 2 diabetes (2019) NICE technology appraisal guidance 572. Review date 2022. Dapagliflozin in triple therapy for treating type 2 diabetes (2016) NICE technology appraisal guidance 418. Review date 2019. Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes (2016) NICE technology appraisal guidance 390. Review date May 2019. Empagliflozin in combination therapy for treating type 2 diabetes (2015, reviewed 2018) NICE technology appraisal guidance 336. Static guidance list. Canagliflozin in combination therapy for treating type 2 diabetes (2014, reviewed 2017) NICE technology appraisal guidance 315. Static guidance list. Dapagliflozin in combination therapy for treating type 2 diabetes (2013, updated 2016) NICE technology appraisal guidance 288. **Related Guidelines:**

	Type 2 diabetes in adults: management (2015, updated 2022) NICE Guideline NG28. **Related Quality Standards:** Diabetes in adults. NICE Quality Standard No. 6, Mar 2011, updated 2016
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 9: Adult specialist endocrinology services, Chapter 67: Insulin-resistant diabetes service (adults and children).

Questions for consultation

Where do you consider tirzepatide will fit into the existing care pathway for type 2 diabetes?

Would tirzepatide be a candidate for managed access?

Do you consider tirzepatide 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 tirzepatide can result in any potential 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 committee to take account of these benefits.

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 tirzepatide 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-

guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

NICE's health technology evaluations: the manual 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. NHS Diabetes. Accessed January 2022
2. Diabetes UK Complications of diabetes. Accessed January 2022
3. Diabetes UK Diabetes and heart disease. Accessed January 2022
4. Diabetes UK Diabetes prevalence 2019. Accessed January 2022
5. Diabetes.co.uk Diabetes prevalence. Accessed January 2022
6. Diabetes UK Ethnicity and type 2 diabetes. Accessed January 2022