

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Evaluation

### Tirzepatide for treating type 2 diabetes

#### Final scope

#### Final 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)<sup>1</sup>. If not managed effectively, diabetes mellitus can lead to kidney failure, blindness, foot problems, and damage to the nervous system<sup>2</sup>. People with diabetes are also more at risk of cardiovascular disease<sup>3</sup>.

There were 3.3 million people in England with diagnosed diabetes mellitus in 2019, of which around 90% had type 2 diabetes<sup>4</sup>. However, an estimated 1 million further people have undiagnosed type 2 diabetes in the UK<sup>4</sup>. The UK prevalence of type 2 diabetes is rising, which has been linked to an increasing prevalence of obesity<sup>5</sup>. 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<sup>6</sup>.

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.

<b>Intervention(s)</b>	Tirzepatide alone or with other antidiabetic agents
<b>Population(s)</b>	<p>Tirzepatide monotherapy:</p> <ul style="list-style-type: none"> <li>• Adults with type 2 diabetes that is inadequately controlled with diet and exercise alone and in whom the use of metformin is considered inappropriate</li> </ul> <p>Tirzepatide with other antidiabetic agents:</p> <ul style="list-style-type: none"> <li>• Adults with type 2 diabetes that is inadequately controlled with one or more antidiabetic agents</li> </ul>
<b>Comparators</b>	<p>The following interventions as monotherapy or in combination regimens, in accordance with NICE guidance:</p> <ul style="list-style-type: none"> <li>• sulfonylureas</li> <li>• DPP-4 inhibitors</li> <li>• pioglitazone</li> <li>• GLP-1 mimetics</li> <li>• SGLT-2 inhibitors</li> <li>• insulin</li> </ul>

<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• HbA1c/glycaemic control</li> <li>• complications of diabetes, including cardiovascular, renal and eye</li> <li>• mortality</li> <li>• body mass index</li> <li>• frequency and severity of hypoglycaemia</li> <li>• changes in cardiovascular risk factors</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p>
<b>Other considerations</b>	<p>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.</p>
<b>Related NICE recommendations and NICE Pathways</b>	<p><b>Related Technology Appraisals:</b></p> <p><a href="#">Ertugliflozin with metformin and a dipeptidyl peptidase-4 inhibitor for treating type 2 diabetes</a> (2019) NICE technology appraisal guidance 583. Review date 2022.</p> <p><a href="#">Ertugliflozin as monotherapy or with metformin for treating type 2 diabetes</a> (2019) NICE technology appraisal guidance 572. Review date 2022.</p> <p><a href="#">Dapagliflozin in triple therapy for treating type 2 diabetes</a> (2016) NICE technology appraisal guidance 418. Review date 2019.</p>

	<p><a href="#">Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes</a> (2016) NICE technology appraisal guidance 390. Review date May 2019.</p> <p><a href="#">Empagliflozin in combination therapy for treating type 2 diabetes</a> (2015, reviewed 2018) NICE technology appraisal guidance 336. Static guidance list.</p> <p><a href="#">Canagliflozin in combination therapy for treating type 2 diabetes</a> (2014, reviewed 2017) NICE technology appraisal guidance 315. Static guidance list.</p> <p><a href="#">Dapagliflozin in combination therapy for treating type 2 diabetes</a> (2013, updated 2016) NICE technology appraisal guidance 288.</p> <p><b>Related Guidelines:</b></p> <p><a href="#">Type 2 diabetes in adults: management</a> (2015, updated 2022) NICE Guideline NG28.</p> <p><b>Related Quality Standards:</b></p> <p><a href="#">Diabetes in adults</a>. NICE Quality Standard No. 6, Mar 2011, updated 2016</p>
<b>Related National Policy</b>	<p>The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2018/2019) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a> Chapter 9: Adult specialist endocrinology services, Chapter 67: Insulin-resistant diabetes service (adults and children).</p>

## 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