National Institute for Health and Care Excellence

Health Technology Evaluation

Tirzepatide for treating type 2 diabetes ID3938
Response to stakeholder organisation comments on the draft remit and draft scope

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Eli Lilly	Yes, this is an appropriate topic to refer to NICE for Single Technology Appraisal.	Thank you for your comment. No changes to scope required.
Wording	Eli Lilly	Yes, the remit broadly reflects the clinical and cost effectiveness of tirzepatide for the treatment of adults with type 2 diabetes (T2D)	Thank you for your comment. No changes to scope required.
Additional comments on the draft remit	Eli Lilly	Tirzepatide represents a step-change in T2D management, and therefore this appraisal should be prioritised. Across the Phase 3 clinical trials, tirzepatide at all doses (5mg, 10mg and 15mg) demonstrated superior and unprecedented glucose lowering and weight loss versus placebo, semaglutide SC 1.0mg, tightly titrated insulin degludec and tightly titrated insulin glargine. HbA1c lowering and weight loss are two of the most important outcome measures in T2D.	Thank you for your comment. This appraisal has been scheduled into the work programme.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Eli Lilly	This section broadly captures the background information of T2D; however Lilly would like to highlight the following important points: • 90% of adults with T2D are overweight or obese[1] There is a positive and statistically significant association between excess body weight and inadequate glycaemic control[2]	Thank you for your comment. The background section of the scope is only intended to briefly describe the disease in the remit, prognosis associated with the condition, epidemiology and treatments currently used in the NHS. No action required.
	Novo Nordisk	The background correctly notes the updated NG28 recommendations which were focused on assessing cardiovascular outcomes.	Thank you for your comment. No changes to scope required.
Population	Eli Lilly	The population in the draft scope has been defined appropriately.	Thank you for your comment. No changes to scope required.
	Novo Nordisk	Given the recently updated NG28 guideline provided recommendations for people with type 2 diabetes with chronic heart failure, cardiovascular disease or at high risk of cardiovascular disease, we believe this population should also be in scope in this assessment.	Thank you for your comment. The population section is inclusive of subgroups such as these and so

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		In the NG28 Consultation on draft guideline – stakeholder comments table, NICE noted in multiple responses (e.g., NICE comments table on page 408) that this was a “priority area...[it] reflected the changing evidence base as a result of the significant investment in clinical trials to directly capture cardiovascular outcomes, feedback from stakeholders that assessing this evidence was a priority and the impact that this new evidence could have on recommendations for the treatment of people with diabetes.” Therefore, we believe this population should be added to the assessment. Proposed additional population: • Adults with type 2 diabetes with chronic heart failure, cardiovascular disease or at high risk of cardiovascular disease We are concerned that if this population is not considered this then leads to an inconsistency in the approach to medicines assessments in type 2 diabetes and does not support clinicians making informed decisions.	are within scope. No action required.
Subgroups	Eli Lilly	None	Comment noted. No change to scope required.
Comparators	Eli Lilly	The monotherapy comparators listed provide a comprehensive reference of standard treatment currently used in the NHS. For the combination therapy comparators list, please add metformin; the list is otherwise comprehensive.	Thank you for your comment. Metformin has not been added to the list of comparators because people having combination therapy would already be having metformin.

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Outcomes	Eli Lilly	Weight loss may be a more appropriate measure as an outcome than BMI, as it is more commonly used as an endpoint in T2D clinical trials. The outcome measures presented otherwise capture the most important health-related benefits of tirzepatide.	Thank you for your comment. Weight loss can be considered within this outcome at appraisal stage. However, for the purposes of the scope, BMI is considered more reflective of the aim of this outcome. That is, to capture movement towards a healthy weight. No action required.
	Novo Nordisk	Given the tolerability profile of the different doses of tirzepatide and the potential dose escalation time, the full implications of these on patients taking the medication should be included in the model in the form of: • Utilities decrements of adverse events (AEs) • Costs associated with treating the AEs • Healthcare resource use required for full dose escalation • Discontinuation of treatment due to AEs	Thank you for your comment. Adverse effects of treatment is included as an outcome in the scope. Utilities, costs and healthcare resources should be captured in the economic model as specified in NICE health technology evaluations: the manual.

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Equality	Eli Lilly	There are no specific limitations identified that might impact access of the treatment for specific subgroups.	Thank you for your comment. No change to the scope required.
Questions for consultation	Eli Lilly	Q1) Where do you consider tirzepatide will fit into the existing care pathway for type 2 diabetes? Tirzepatide is anticipated to be used at the point of treatment intensification according to NICE T2D NG28, in both primary and secondary care. Q2) Would tirzepatide be a candidate for managed access? Tirzepatide is expected to be made available for routine commissioning. Managed access is not expected to be considered in the appraisal. Q3) 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)? Yes. Across the Phase 3 clinical trials, tirzepatide at all doses (5mg, 10mg and 15mg) demonstrated superior and unprecedented glucose lowering and weight loss versus placebo, semaglutide SC 1.0mg, tightly titrated insulin degludec and tightly titrated insulin glargine. HbA1c lowering and weight loss are two of the most important outcome measures in T2D.	Thank you for your comments. 1) No change to the scope required. 2) No change to the scope required. 3) The innovative nature of tirzepatide will be considered by the committee throughout the appraisal. 4) The committee will consider the health-related quality of life and any potential uncaptured benefits throughout the appraisal.

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		Q4) 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? In addition to glycaemic control, ADA and EASD consensus guidelines recommend weight management for patients with T2D who are obese or overweight.3, 4 The health-related benefits of weight loss and patient quality of life is significant and associated with improvements in weight related patient-reported outcomes (PROs), such as Ability to Perform Physical Activities of Daily Living (APPADL), Impact of Weight on Quality of Life-Lite Clinical Trials (IWQOL-Lite-CT), and Impact of Weight on Self-Perceptions (IW-SP) with particular improvement seen in patients' physical functioning. These PRO improvements are all unlikely to be fully captured in the QALY calculation. Also, there is evidence to suggest regardless of therapy, higher percentages of weight loss in patients with T2D would have greater improvements in PRO scores. The anticipated benefits of tirzepatide treatment on cardiovascular outcomes, particularly in patients with high cardiovascular disease risk, are also unlikely to be fully captured in the QALY calculation for this submission. This is because the cardiovascular outcomes trial that will provide evidence for tirzepatide in these outcomes is currently ongoing with anticipated completion in 2025, after this appraisal will have concluded. **References** 1. Public Health England. Adult obesity and type 2 diabetes. 2014. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/u	

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		ploads/attachment_data/file/338934/Adult_obesity_and_type_2_diabetes_.pdf/ [Last accessed: 30 March 2022]. 2. Bae JP, Lage MJ, Mo D, et al. Obesity and glycemic control in patients with diabetes mellitus: Analysis of physician electronic health records in the US from 2009-2011. J Diabetes Complications 2016;30:212-20. 3. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. Diabetes Care 2020;43:S14-s31. 4. Buse JB, Wexler DJ, Tsapas A, et al. 2019 update to: Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia 2020;63:221-228.	