NICE National Institute for Health and Care Excellence

Tirzepatide: local formulary information

Implementation support
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Contents

Purpose

NICE's medicines practice guideline on developing and updating local formularies recommends that medicines recommended in NICE technology appraisals are adopted into local formularies automatically (if clinically appropriate and relevant to the services provided by the organisation). This document supports that process by summarising information that local formulary decision-making groups are likely to need.

Local groups have their own formats of multi-criteria decision tool, reflecting their needs. This document is not intended to mandate any change or variation from those. Local groups can use this resource to help complete their own local documents, adapting it to their own circumstances and supplementing it with additional information as necessary.

Medicine name and product details

Tirzepatide (Mounjaro, Eli Lilly) is a long-acting dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist for subcutaneous injection with a pre-filled pen. It is licensed for weight management as an adjunct to a reduced-calorie diet and increased physical activity in adults with specified initial body mass index (BMI). The details of the licensed indication and dosage schedule are available in the summary of product characteristics for tirzepatide.

National guidance and priorities

NICE technology appraisal guidance TA1026 states:

1.1 Tirzepatide is recommended as an option for managing overweight and obesity, alongside a reduced-calorie diet and increased physical activity in adults, only if they have:

- an initial body mass index (BMI) of at least 35 kg/m^2 and
- at least 1 weight-related comorbidity.

Use a lower BMI threshold (usually reduced by 2.5 kg/m^2) for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean ethnic backgrounds.

1.2 If less than 5% of the initial weight has been lost after 6 months on the highest tolerated dose, decide whether to continue treatment, taking into account the benefits and risks of treatment for the person.

1.3 These recommendations are not intended to affect treatment with tirzepatide that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.

Tirzepatide is also recommended in NICE technology appraisal guidance 924 as an option for treating type 2 diabetes alongside diet and exercise in certain situations.

Guidance implementation

Prioritisation of cohorts for treatment will be based on a prioritisation statement led by clinical need and produced by NHS England. This will consider both referral prioritisation in specialist weight management services and priority cohorts in other settings, including primary care-based services.

Integrated care boards (ICBs) are required to fund tirzepatide:

- within 3 months for everyone accessing specialist weight management services at that time, and subsequently
- from 6 months to support a phased introduction of delivery to other eligible cohorts.

NHS England has published interim commissioning guidance for NICE TA1026. This details eligible patient cohorts, prioritisation strategy and phased implementation of tirzepatide across specialist weight management services and primary care settings. It also outlines the funding allocations to Integrated Care Boards (ICBs) to ensure effective delivery and equitable access to treatment across NHS systems.

NICE will evaluate data collected during the first phase of guidance implementation, within the first 3 years. It will consider whether to revise the maximum total 12-year implementation period and whether NHS England should produce an updated interim commissioning policy for the remaining implementation period.

Clinical effectiveness

Tirzepatide has been studied in weight management in 2 large, phase 3 studies: SURMOUNT-1 (n=2,539) in people who did not have diabetes and SURMOUNT-2 (n=938) in people with type 2 diabetes. Both trials had a similar design and the same co-primary endpoints: the percentage change in body weight from baseline to week 72 and a weight reduction of 5% or more at week 72. The 72-week treatment period included a dose-escalation phase. Tirzepatide was started at a dose of 2.5 mg once weekly (or matching placebo) and the dose was increased by 2.5 mg every 4 weeks until the target dose was reached. In both trials, people in all the study arms had lifestyle counselling sessions, delivered by a dietitian or other qualified healthcare professional. These were to help them adhere to healthy, balanced meals with a deficit of 500 calories per day, and at least 150 minutes of physical activity per week.

People without diabetes

SURMOUNT-1 included people with a BMI of 30 kg/m^2 or more, or 27 kg/m^2 or more and at least 1 weight-related complication (excluding diabetes). The mean baseline BMI was 38.0 kg/m^2 (35% of people in the trial had a BMI 30 to 34 kg/m^2, 28% had a BMI 35 to 39 kg/m^2 and 32% had a BMI 40 kg/m^2 or more). People were randomised in equal numbers to tirzepatide 5 mg weekly, 10 mg weekly or 15 mg weekly, or placebo.

Evidence on tirzepatide's treatment effect compared with placebo in the population covered by the technology appraisal recommendation (BMI of at least 35 kg/m^2 and at least 1 weight-related comorbidity) was provided to NICE in confidence. Published results from the whole trial intention-to-treat population (treatment estimand) are shown in table 1. This treatment estimand represents the average treatment effect of tirzepatide relative to placebo for everyone who was randomised, regardless of treatment discontinuation.

Table 1 Effects of tirzepatide on body weight and BMI at 72 weeks in SURMOUNT-1 (means and 95% confidence intervals)

Outcome	Tirzepatide 5 mg	Tirzepatide 10 mg	Tirzepatide 15 mg	Placebo
Percentage reduction in body weight	15.0% (14.2% to 15.9%)	19.5% (18.5% to 20.4%)	20.9% (19.9% to 21.8%)	3.1% (1.9% to 4.3%)

Outcome	Tirzepatide 5 mg	Tirzepatide 10 mg	Tirzepatide 15 mg	Placebo
Weight reduction of 5% or more	85.1% (81.6% to 88.6%)	88.9% (85.9% to 91.9%)	90.9% (88.0% to 93.8%)	34.5% (29.8% to 39.2%)
Weight reduction of 10% or more	68.5% (64.5% to 72.5%)	78.1% (74.4% to 81.7%)	83.5% (80.0% to 86.9%)	18.8% (14.9% to 22.7%)
Weight reduction of 15% or more	48.0% (43.9% to 52.1%)	66.6% (62.6% to 70.6%)	70.6% (66.7% to 74.5%)	8.8% (5.9% to 11.7%)
Weight reduction of 20% or more	30.0% (26.4% to 33.6%)	50.1% (46.0% to 54.2%	56.7% (52.6% to 60.8%)	3.1% (1.1% to 5.1%)

People with diabetes

SURMOUNT-2 included people with a BMI of 27 kg/m^2 or more and type 2 diabetes (HbA1c 53 to 86 mmol/mol on stable therapy, excluding DPP-4 inhibitors, GLP-1 agonists or any other injectable treatment for diabetes). The mean baseline BMI was 36.1 kg/m^2; 17% had a BMI less than 30 kg/m^2, 33% had a BMI between 30 and less than 35 kg/m^2, and roughly equal proportions of the remaining half had a BMI between 35 to less than 40 kg/m^2 and 40 kg/m^2 or more. People were randomised in equal numbers to tirzepatide 10 mg weekly or 15 mg weekly, or placebo.

Published results from the whole trial intention-to-treat population (treatment estimand) are shown in table 2.

Table 2 Effects of tirzepatide on body weight and BMI at 72 weeks in SURMOUNT-2 (95% confidence intervals not stated in study report)

Outcome	Tirzepatide 10 mg	Tirzepatide 15 mg	Placebo
Percentage reduction in body weight	12.8%	14.7%	3.2%
Weight reduction of 5% or more	79%	83%	32%
Weight reduction of 10% or more	61%	65%	9%
Weight reduction of 15% or more	40%	48%	3%

Outcome	Tirzepatide 10 mg	Tirzepatide 15 mg	Placebo
Weight reduction of 20% or more	22%	31%	1%

Patient safety

Contraindications, warnings, precautions for use and reported adverse effects are available in the summary of product characteristics for tirzepatide.

Adverse effects

In SURMOUNT-1 and SURMOUNT-2, 2,519 people had tirzepatide alone or in combination with other glucose-lowering medicines. The most frequently reported adverse reactions were gastrointestinal disorders, including nausea, diarrhoea, constipation and vomiting (see table 3). In general, these reactions were mostly mild or moderate in severity and occurred more often during dose escalation and decreased over time.

Table 3 Gastrointestinal adverse effects reported in phase 3 studies of weight management

Adverse effect	Tirzepatide (no type 2 diabetes)	Placebo (no type 2 diabetes)	Tirzepatide (with type 2 diabetes)	Placebo (with type 2 diabetes)
Nausea	30%	9%	21%	6%
Vomiting	10%	2%	12%	3%
Diarrhoea	21%	7%	21%	9%
Constipation	15%	6%	9%	4%
Dyspepsia	10%	4%	7%	3%
Abdominal pain	5%	3%	6%	2%
Eructation	5%	1%	5%	1%

Pancreatitis has been reported with tirzepatide and other GLP-1 agonists. In SURMOUNT-1 and SURMOUNT-2 pancreatitis was reported in only a small number of people. However, the trials were not powered to detect a difference between the tirzepatide and placebo groups and are unlikely to give reliable estimates of absolute or comparative risks. In people who did not have diabetes, hypoglycaemia was reported more frequently with tirzepatide than with placebo.

Pregnancy and contraception

Tirzepatide is not recommended during pregnancy or in people who can become pregnant and who are not using contraception. If the person wishes to become pregnant, tirzepatide should be stopped at least 1 month before a planned pregnancy because of its long half-life.

There is limited information about the effect of tirzepatide on the pharmacokinetics and efficacy of oral contraceptives in people with overweight or obesity. Since reduced efficacy of oral contraceptives cannot be excluded, switching to a non-oral contraceptive method, or adding a barrier method of contraception, is advised for 4 weeks after starting treatment and after each dose escalation (see the summary of product characteristics for tirzepatide).

Other risk groups

Tirzepatide's gastrointestinal adverse effects could lead to dehydration and in turn a deterioration in renal function including acute renal failure. Older people and some other groups of people may be more susceptible to such complications (see the summary of product characteristics for tirzepatide). People at risk of falls may be at further risk if they experience hypoglycaemia.

Place in the treatment pathway relative to other available treatments

Tirzepatide should be thought about as an option for individual people in line with NICE's guideline on overweight and obesity management. The visual summary potential care journey has an overview.

Table 4 is also available in section 1.17 of NICE's guideline on overweight and obesity management.

Table 4 medicines options for weight management in adults

-	Tirzepatide	Semaglutide	Liraglutide	Orlistat
For more details see	NICE's technology appraisal guidance on tirzepatide for managing overweight and obesity (TA1026, December 2024)	NICE's technology appraisal guidance on semaglutide for managing overweight and obesity (TA875, March 2023)	NICE's technology appraisal guidance on liraglutide for managing overweight and obesity (TA664, December 2020)	There is no NICE technology appraisal guidance on orlistat

-	Tirzepatide	Semaglutide	Liraglutide	Orlistat
For people with	An initial BMI of at least 35 kg/m^2 and at least 1 weight-related comorbidity.	At least 1 weight-related comorbidity **and**: • an initial BMI of 35.0 kg/m^2 or more, **or** • an initial BMI of 30.0 kg/m^2 to 34.9 kg/m^2 and who meet the criteria for referral to specialist overweight and obesity management services.	An initial BMI of 35 kg/m^2 or more **and** non-diabetic hyperglycaemia **and** a high risk of cardiovascular disease.	A BMI of 30 kg/m^2 or more **or** a BMI of 28 kg/m^2 or more and associated risk factors. (orlistat summary of product characteristics [SPC])
Setting	Prescribed in primary care or a specialist overweight and obesity management service..	Prescribed in a specialist overweight and obesity management service.	Prescribed in secondary care by a specialist overweight and obesity management service.	Prescribed in all settings and available in a lower dose from a pharmacy.
Route and frequency	Weekly subcutaneous injection.	Weekly subcutaneous injection.	Daily subcutaneous injection.	Oral capsule, up to 3 times a day.

-	Tirzepatide	Semaglutide	Liraglutide	Orlistat
Pregnancy and contraception	Do not use in pregnancy or in women of childbearing potential not using contraception. Switch to a non-oral contraceptive method, or add a barrier method of contraception, for 4 weeks on initiation and after each dose escalation. (tirzepatide SPC)	Do not use in pregnancy. Women of childbearing potential are recommended to use contraception. (semaglutide SPC)	Do not use in pregnancy. (liraglutide SPC)	Caution in pregnancy. The use of an additional contraceptive method is recommended to prevent possible failure of oral contraception that could occur in case of severe diarrhoea. (orlistat SPC)
When to stop treatment	If less than 5% of the initial weight has been lost after 6 months on the highest tolerated dose, decide whether to continue treatment, taking into account the benefits and risks of treatment for the person.	Consider stopping if less than 5% of the initial weight has been lost after 6 months of treatment.	Stop after 12 weeks on the 3.0 mg/day dose if at least 5% of the initial body weight has not been lost. (liraglutide SPC)	Stop after 12 weeks if at least 5% of the initial body weight has not been lost. (orlistat SPC)

The guideline defines specialist overweight and obesity management services as specialist primary, community or secondary care-based services led by a multidisciplinary team, offering a combination of nutritional, psychological and surgical interventions, and medicines. These services can include but are not limited to tier 3 and tier 4 services.

Semaglutide and liraglutide are recommended for use within specialist weight management services, which are usually accessed for up to 2 years.

For tirzepatide, semaglutide and liraglutide, use lower BMI thresholds (usually reduced by 2.5 kg/m^2) for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean ethnic backgrounds.

Non-diabetic hyperglyacaemia is defined as a haemoglobin A1c level of 42 mmol/mol to 47 mmol/mol (6.0% to 6.4%) or a fasting plasma glucose level of 5.5 mmol/litre to 6.9 mmol/litre.

Naltrexone-bupropion is not recommended in NICE's technology appraisal guidance on naltrexone–bupropion for managing overweight and obesity in adults.

NICE's early value assessment on digital technologies for delivering multidisciplinary weight-management services covers technologies that can be used in the NHS, while more evidence is generated. They can be used to prescribe and monitor weight-management medicines and deliver multidisciplinary weight-management services.

The local formulary decision-making group will need to agree on where tirzepatide will be started locally, and arrangements for ongoing prescription.

Resource impact

NICE has produced a resource impact assessment tool for tirzepatide.

NICE estimates that the total eligible population is 3.4 million people, and expects that an interim NHS England commissioning policy will identify at least 220,000 people in England eligible for tirzepatide to be funded within the first 3 years of implementation.

References

1. Jastreboff A, Aronne L, Ahmad N, et al. (2022) Tirzepatide once weekly for the treatment of obesity. New Eng J Med 387: 205–16 (SURMOUNT-1)

2. Garvey W, Frias J, Jastreboff A, et al. (2023) Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet 402: 613–26

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