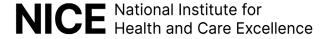
Tirzepatide

A discussion aid for healthcare professionals and patients

One of the tools and resources for the NICE guideline on overweight and obesity management (NG246)



What is this document for?

This discussion aid is provided to support discussions between healthcare professionals and people considering tirzepatide treatment.

Healthcare professionals should refer to the <u>summary of product characteristics</u> for full prescribing information. People considering treatment should also see the manufacturer's patient information leaflet.



In summary:

- Adding tirzepatide is more effective than diet and exercise alone at reducing body weight,
 while on treatment.
- People who stop tirzepatide are likely to regain the weight they had lost, but there is no long-term data for what happens to weight after stopping it. With a similar medicine, people usually regain weight lost during treatment within 2 years of stopping it, and weight regain is likely to be greatest in the first year after stopping.
- Many people experience gastrointestinal effects, though not everyone does. These are reported to be mostly mild or moderate in severity, occur more often during dose escalation and decrease over time.
- The risks of rare but serious side effects, and the long-term effects on health and nutrition, are not yet known.
- Tirzepatide should not be used in pregnancy and can reduce the effectiveness of oral contraceptives.
- Tirzepatide does not take away the need for a healthy, balanced, weight-reducing diet, plus increased activity. There are wider health benefits from increased activity and healthier diet, which should be considered.

What does treatment involve?

Tirzepatide is given by injection once a week. The person injects themselves under the skin of their abdomen, thigh or upper arm (see the <u>manufacturer's user manual</u>). Treatment starts at 2.5 mg once a week for 4 weeks. This can be increased by 2.5 mg once a week every 4 weeks, to a maximum of 15 mg once a week.

Tirzepatide works mainly by regulating the person's appetite, giving them a sense of fullness (satiety). They feel less hungry and experience fewer food cravings. This helps them eat less food and reduce their body weight.

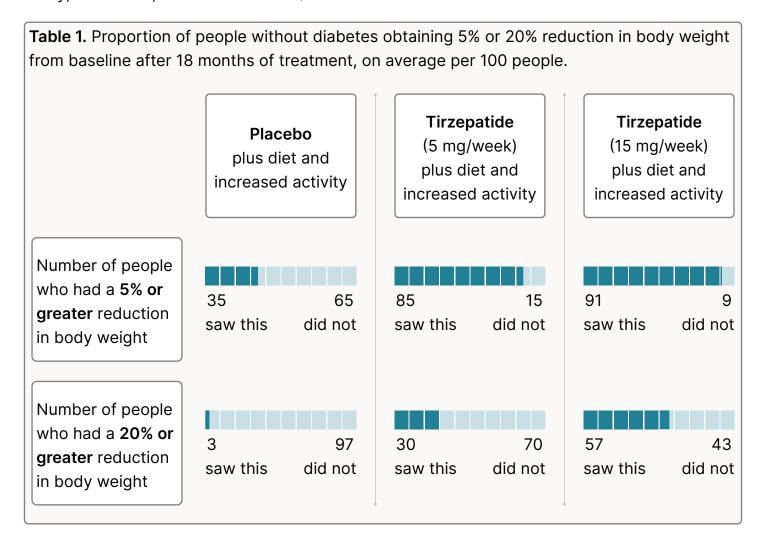
What are the potential benefits?

All the people in the studies whose results are shown here had counselling sessions from a healthcare professional to help them follow a diet of healthy, balanced meals with a deficit of 500 calories a day, and undertake at least 150 minutes of physical activity a week.

<u>Appendix 1</u> shows body weight after a 5% and 20% reduction, for a range of initial body weights. <u>Appendix 2</u> provides links to tools for assessing overweight and obesity.

People without diabetes

An 18-month study in 2,539 people who were living with overweight or obesity and who did not have diabetes compared tirzepatide at different doses with placebo (the SURMOUNT-1 study; Jastreboff, Aronne et al. 2022).



People with diabetes

An 18-month study in 938 people who were living with overweight or obesity and who also had diabetes compared tirzepatide at two different doses with placebo (the SURMOUNT-2 study; Garvey, Frias et al. 2022).

Table 2. Proportion of people with diabetes obtaining 5% or 20% reduction in body weight from baseline after 18 months of treatment, on average per 100 people. Tirzepatide Tirzepatide **Placebo** (10 mg/week) (15 mg/week) plus diet and plus diet and plus diet and increased activity increased activity increased activity Number of people who had a 5% or 32 68 79 21 83 17 greater reduction did not saw this saw this did not saw this did not in body weight Number of people who had a 20% or 99 22 78 31 69 greater reduction saw this saw this did not saw this did not did not in body weight



Stopping treatment and weight regain

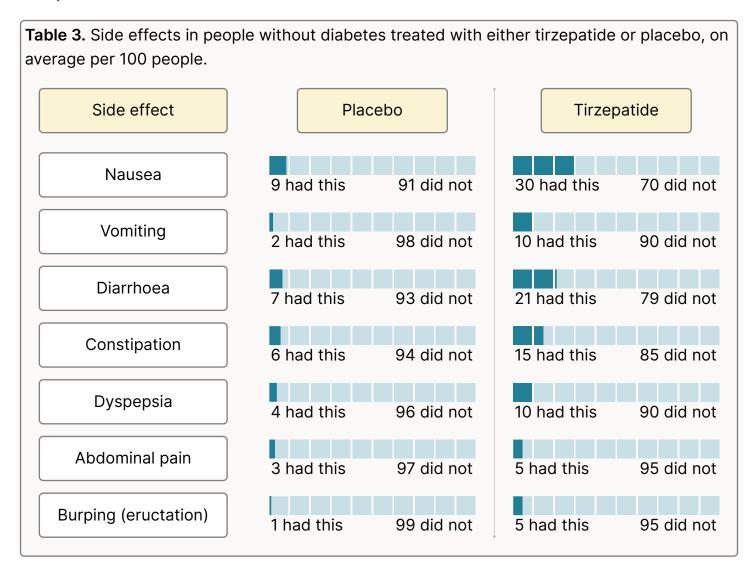
If a person has lost less than 5% of their original body weight after 6 months on the highest tolerated dose, decide whether to continue treatment, taking into account the benefits and risks of treatment for the person. <u>Appendix 1</u> shows body weight after a 5% and 20% reduction, for a range of initial body weights. <u>Appendix 2</u> provides links to tools for assessing overweight and obesity.

People who stop tirzepatide are likely to regain weight they had lost, but there is no long-term data for what happens to weight after stopping it. In its appraisal of tirzepatide, NICE noted that with a similar medicine, semaglutide, people usually regain the weight they have lost by about 2 years after stopping it. Around two thirds of the weight lost while on treatment is regained within the first year after stopping treatment (NICE technology appraisal TA1026).

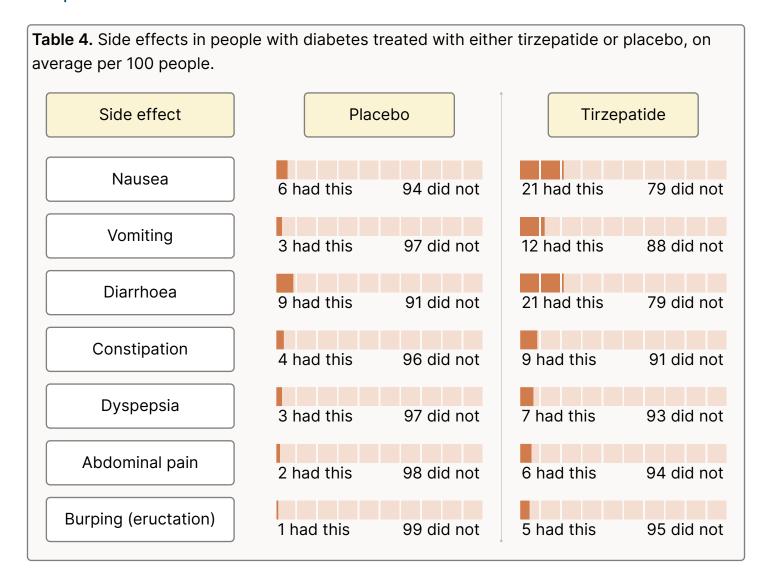
What are the potential harms and unwanted effects? Side effects

In the studies (SURMOUNT-1 and SURMOUNT-2), gastrointestinal disorders were the most commonly reported side effects, including nausea, diarrhoea, constipation and vomiting (Jastreboff, Aronne et al. 2022; Garvey, Frias et al. 2022). In general, these were mostly mild or moderate; they occurred more often during dose escalation and decreased over time. However, they may lead to dehydration which could potentially cause acute kidney injury (see the summary of product characteristics). People prescribed tirzepatide should be advised about this; the NHS page on acute kidney injury may be helpful to share.

People without diabetes



People with diabetes



Other side effects reported in the studies included:

- hair loss (mainly mild): 5 people in 100 on tirzepatide got this (so 95 did not),
 compared with 1 person in 100 on placebo (so 99 did not)
- rashes
- injection site reactions.

Pancreatitis

Acute pancreatitis has occurred in people treated with tirzepatide, but the frequency of this is unclear. People prescribed tirzepatide should be told about the symptoms of acute pancreatitis and advised to seek urgent medical advice if they experience them (see the NHS page on acute pancreatitis for information suitable for sharing).

If pancreatitis is suspected, tirzepatide should be stopped and not restarted if the diagnosis is confirmed (see the <u>summary of product characteristics</u>).

Safety in pregnancy and effects on contraception

Tirzepatide should not be used in pregnancy and is not recommended in people who could become pregnant unless they are using contraception. Tirzepatide should be stopped at least 1 month before a planned pregnancy, because of its long half-life (see the <u>summary of product characteristics</u>).

People taking oral contraceptives should switch to a non-oral contraceptive method, or add a barrier method of contraception, for 4 weeks after starting treatment and after each dose increase (see the <u>summary of product characteristics</u>).

Other potential harms

The risks of other rare but serious side effects, and the long-term effects on health and nutrition from using tirzepatide are not yet known.

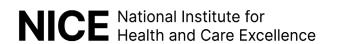
Alternatives to tirzepatide

Other pharmacological options may be suitable for the person if tirzepatide is not, depending on their circumstances. For information on these and wider aspects of care for people living with overweight or obesity, see the NICE guideline on overweight and obesity. and the NICE practical guide to using medicines to manage overweight and obesity.

People may wish to review, continue or increase their current non-pharmacological approaches to weight management instead of starting tirzepatide or other medicines. Pharmacological approaches do not take away the need for a healthy, balanced, weight-reducing diet, plus increased activity. In studies, about a third of people saw a 5% or greater reduction in weight from these alone (so about two thirds did not): see the <u>section on potential benefits</u>. There are also wider health benefits from increased activity, which should be considered.

References

- 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(10402): 613–26.
- Jastreboff A, Aronne L, Ahmad N, et al. (2022) Tirzepatide once weekly for the treatment of obesity. New Eng J Med 387(3): 205–16. (SURMOUNT-1)
- Overweight and obesity management (2025). NICE guideline NG246.
- <u>Tirzepatide for managing overweight and obesity</u> (2024). NICE technology appraisal guidance 1026.



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Appendix 1: 5% and 20% reductions in body weight

5	A.C. FO/	A C C C C C C C C C C		A.S. = 50/	A 51
Baseline body	After a 5%	After a 20%	Baseline body	After a 5%	After a 20%
weight (kg)	reduction	reduction	weight (st lbs)	reduction	reduction
75 kg	71 kg	60 kg	11 st 11 lbs	11 st 3 lbs	9 st 6 lbs
77 kg	73 kg	62 kg	12 st 2 lbs	11 st 7 lbs	9 st 10 lbs
79 kg	75 kg	63 kg	12 st 6 lbs	11 st 11 lbs	9 st 13 lbs
81 kg	77 kg	65 kg	12 st 11 lbs	12 st 2 lbs	10 st 3 lbs
83 kg	79 kg	66 kg	13 st 1 lbs	12 st 6 lbs	10 st 6 lbs
85 kg	81 kg	68 kg	13 st 5 lbs	12 st 10 lbs	10 st 10 lbs
87 kg	83 kg	70 kg	13 st 10 lbs	13 st 0 lbs	10 st 13 lbs
89 kg	85 kg	71 kg	14 st 0 lbs	13 st 4 lbs	11 st 3 lbs
91 kg	86 kg	73 kg	14 st 5 lbs	13 st 9 lbs	11 st 6 lbs
93 kg	88 kg	74 kg	14 st 9 lbs	13 st 13 lbs	11 st 10 lbs
95 kg	90 kg	76 kg	14 st 13 lbs	14 st 3 lbs	12 st 0 lbs
97 kg	92 kg	78 kg	15 st 4 lbs	14 st 7 lbs	12 st 3 lbs
99 kg	94 kg	79 kg	15 st 8 lbs	14 st 11 lbs	12 st 7 lbs
101 kg	96 kg	81 kg	15 st 13 lbs	15 st 2 lbs	12 st 10 lbs
103 kg	98 kg	82 kg	16 st 3 lbs	15 st 6 lbs	13 st 0 lbs
105 kg	100 kg	84 kg	16 st 7 lbs	15 st 10 lbs	13 st 3 lbs
107 kg	102 kg	86 kg	16 st 12 lbs	16 st 0 lbs	13 st 7 lbs
109 kg	104 kg	87 kg	17 st 2 lbs	16 st 4 lbs	13 st 10 lbs
111 kg	105 kg	89 kg	17 st 7 lbs	16 st 8 lbs	14 st 0 lbs
113 kg	107 kg	90 kg	17 st 11 lbs	16 st 13 lbs	14 st 3 lbs
115 kg	109 kg	92 kg	18 st 2 lbs	17 st 3 lbs	14 st 7 lbs
117 kg	111 kg	94 kg	18 st 6 lbs	17 st 7 lbs	14 st 10 lbs
119 kg	113 kg	95 kg	18 st 10 lbs	17 st 11 lbs	15 st 0 lbs
121 kg	115 kg	97 kg	19 st 1 lbs	18 st 1 lbs	15 st 3 lbs
123 kg	117 kg	98 kg	19 st 5 lbs	18 st 6 lbs	15 st 7 lbs
125 kg	119 kg	100 kg	19 st 10 lbs	18 st 10 lbs	15 st 10 lbs
127 kg	121 kg	102 kg	20 st 0 lbs	18 st 14 lbs	16 st 0 lbs
129 kg	123 kg	103 kg	20 st 4 lbs	19 st 4 lbs	16 st 4 lbs
131 kg	124 kg	105 kg	20 st 9 lbs	19 st 8 lbs	16 st 7 lbs
133 kg	126 kg	106 kg	20 st 13 lbs	19 st 13 lbs	16 st 11 lbs
135 kg	128 kg	108 kg	21 st 4 lbs	20 st 3 lbs	17 st 0 lbs
137 kg	130 kg	110 kg	21 st 8 lbs	20 st 7 lbs	17 st 4 lbs
139 kg	132 kg	111 kg	21 st 12 lbs	20 st 11 lbs	17 st 7 lbs
141 kg	134 kg	113 kg	22 st 3 lbs	21 st 1 lbs	17 st 11 lbs
143 kg	136 kg	114 kg	22 st 7 lbs	21 st 5 lbs	18 st 0 lbs
145 kg	138 kg	116 kg	22 st 12 lbs	21 st 10 lbs	18 st 4 lbs

Appendix 2: Useful measurements

Body mass index (BMI) calculator

The <u>NHS BMI calculator</u> can be used to work out if a person is in a healthy weight range for their height. There is a version for adults, and one for children and teenagers. The BMI calculator should not be used in pregnancy, by people with eating disorders, or by people with conditions that affect their height.

The calculator will ask for some details such as height, weight, and ethnic background.

A person's BMI is just one measurement and can be less accurate in some people than others (for example, people with more muscle as this is heavier).

Other measures and factors

A person's waist circumference and waist to height ratio can be useful to work out if they are carrying too much weight around their middle (this is called central adiposity). A person with a 'healthy' BMI could still be at risk if they have excess weight in this area. People from some ethnic backgrounds are more prone to central adiposity.

The <u>section on identifying and assessing overweight and obesity in adults in the NICE</u> <u>guideline on overweight and obesity management</u> has information on how to correctly measure a person's waist, how to calculate a person's weight to height ratio, and how results should be interpreted for different population groups.