NHS
Cheshire and Merseyside

Tirzepatide for managing overweight and obesity (NICE TA1026)

RED – specialist prescribing

TEMPORARY STATEMENT FOR INITIAL IMPLEMENTATION PERIOD

This temporary red statement applies to the initial 3 month implementation period for patients accessing specialist weight management services.

Recommendations [1]

The Cheshire and Merseyside Area Prescribing Group recommend the prescribing of tirzepetide in accordance with NICE Technology Appraisal (TA) 1026.

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.

Lower BMI thresholds (usually reduced by 2.5 kg/m^2) should be used for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean ethnic backgrounds.

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

Implementation notes [1]

- NHS England submitted a funding variation request, on behalf of NHS providers and ICBs, to extend the time needed to comply with the recommendations in NICE TA1026. This is because a large number of people would potentially be eligible for tirzepatide and the resources needed for its delivery, such as diet and exercise support, are not available equitably across the country.
- NICE considered the funding variation request and recommends mandated funding of tirzepatide as follows:
  - tirzepatide must be made available **within 3 months** from final guidance publication for all patients accessing specialist weight management services at that time and subsequently, since these services and the associated wraparound care is already established.
  - tirzepatide must be made available **from 6 months** from final guidance publication for a phased introduction of delivery to other eligible cohorts in line with NHS England's interim commissioning policy, since NICE accepts that it will take time for commissioners to establish effective services in primary care.

Prescribing information [2]

- Tirzepatide is a glucagon-like peptide-1 receptor agonist (GLP-1RA) combined with glucose-dependent insulinotropic polypeptide receptor agonist (GIP RA). Prescribers should inform patients about the common and serious side effects associated with GLP-1RAs [3]. Refer to MHRA Drug Safety Update .

- The starting dose of tirzepatide is 2.5 mg once weekly. After 4 weeks, the dose should be increased to 5 mg once weekly. If needed, dose increases can be made in 2.5 mg increments after a minimum of 4 weeks on the current dose. The recommended maintenance doses are 5, 10 and 15 mg. The maximum dose is 15 mg once weekly.
- Tirzepatide is to be injected subcutaneously in the abdomen, thigh or upper arm. The dose can be administered at any time of day, with or without meals. Injection sites should be rotated with each dose. If a patient also injects insulin, they should inject tirzepatide into a different injection site.
- When tirzepatide is added to existing metformin and/or sodium-glucose co-transporter 2 inhibitor (SGLT2i) therapy, the current dose of metformin and/or SGLT2i can be continued. Patients receiving tirzepatide in combination with an insulin secretagogue (for example, a sulphonylurea) or insulin may have an increased risk of hypoglycaemia. The risk of hypoglycaemia may be lowered by a reduction in the dose of the insulin secretagogue or insulin.
- Tirzepatide is supplied as one multiple-dose pre-filled KwikPen, which contains 4 doses of 0.6ml to be administered. As tirzepatide is given weekly, each pen lasts for 1 month. The pens need to be stored in a fridge at 2 to 8°C. They can be stored unrefrigerated for up to 30 days at a temperature not above 30°C and then the pre-filled KwikPen must be discarded.

Patient factors [2]

Elderly, gender, race, ethnicity or body weight

No dose adjustment needed. There are only very limited data available from patients aged ≥ 85 years

Renal and hepatic impairment

No dose adjustment is required for patients with renal impairment including end stage renal disease (ESRD) or hepatic impairment. However, experience with the use of tirzepatide in patients with severe renal impairment, ESRD and hepatic impairment is limited and tirzepatide should be used with caution.

Paediatric population

The safety and efficacy of tirzepatide in children aged less than 18 years have not yet been established.

Concomitant medication

Tirzepatide delays gastric emptying and thereby has the potential to impact the rate of absorption of concomitantly administered oral medicinal products. No dose adjustments are expected to be required for most concomitantly administered oral medicinal products. However, it is recommended to monitor patients on oral medicinal products with a narrow therapeutic index (e.g., warfarin, digoxin), especially at initiation of tirzepatide treatment and following dose increase. The risk of delayed effect should also be considered for oral medicinal products for which a rapid onset of effect is of importance.
Since reduced efficacy of oral contraceptives cannot be excluded, it is advised switching to a non-oral contraceptive method, or add a barrier method of contraception upon initiating tirzepatide therapy (for 4 weeks), or after each dose escalation (for 4 weeks).

Fertility, pregnancy and lactation

Tirzepatide is not recommended during pregnancy and in women of childbearing potential not using contraception. If a patient wishes to become pregnant, tirzepatide should be discontinued at least 1 month before a planned pregnancy due to its long half-life.

It is unknown whether tirzepatide is excreted in human milk and a risk to the newborn/infant cannot be excluded. The effect of tirzepatide on fertility in humans is unknown.

Driving and use of machinery

When tirzepatide is used in combination with a sulphonylurea or insulin patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines.

Safety [2]

Refer to SPC for full safety information.

Contraindications/drug interactions

Tirzepatide is contraindicated in those with hypersensitivity to the active substance or to any of the excipients. Patients receiving tirzepatide in combination with an insulin secretagogue (for example, a sulphonylurea) or insulin may have an increased risk of hypoglycaemia. The risk of hypoglycaemia may be lowered by a reduction in the dose of the insulin secretagogue or insulin.

Pancreatitis

Tirzepatide has not been studied in patients with a history of pancreatitis, and should be used with caution in these patients. Acute pancreatitis has been reported in patients treated with tirzepatide and patients should be informed of the symptoms of this. If pancreatitis is suspected, tirzepatide should be discontinued.

Gastrointestinal adverse reactions

Tirzepatide has been associated with gastrointestinal adverse reactions, which include nausea, vomiting and diarrhoea. These adverse reactions may lead to dehydration, which could lead to a deterioration in renal function including acute renal failure. Patients treated with tirzepatide should be advised of the potential risk of dehydration, due to the gastrointestinal adverse reactions and take precautions to avoid fluid depletion and electrolyte disturbances. This should particularly be considered in the elderly, who may be more susceptible to such complications.

Cautions

Tirzepatide has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis, or in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy or diabetic macular oedema, and should be used with caution in these patients.

Cost [4]

The NHS list prices of tirzepatide KwikPen (4-week supply of pre-filled pen devices for subcutaneous injection) are:

- £92.00 for 2.5 mg and 5 mg (cost for 365 days = £1199)
- £107.00 for 7.5 mg and 10 mg (cost for 365 days = £1395)
- £122.00 for 12.5 mg and 15 mg (cost for 365 days = £1590)

The NHS list prices of semaglutide (4-week supply of pre-filled pen devices for subcutaneous injection) are:

- £73.25 for 0.25mg, 0.5mg, and 1mg (cost for 365 days = £955)
- £124.53 for 1.7mg (cost for 365 days = £1623)
- £175.80 for 2.4mg (cost for 365 days = £2291)

  This does not include any commercial arrangement discounts.

Effectiveness [1]

The clinical-effectiveness evidence for tirzepatide comes from the SURMOUNT-1 clinical trial. SURMOUNT-1 was a randomised, double-blind trial that compared tirzepatide with placebo, both alongside diet and exercise support. It included adults with obesity (BMI of 30.0 kg/m^2 or more) with or without a comorbidity, or with overweight (BMI of 27.0 kg/m^2 to 29.9 kg/m^2) with at least 1 weight-related comorbidity. People with type 2 diabetes or with history of severe psychiatric disorders within the last 2 years were excluded. The trial was done in 9 countries but there were no study sites in the UK. The trial included 4 arms: 3 arms were given tirzepatide at either a 5 mg (n=630), 10 mg (n=636), or 15 mg (n=630) dose and 1 arm was given placebo (n=643). All arms were followed up for 72 weeks.

The primary outcomes were mean percentage change in body weight and mean percentage of people with 5% or more body weight reduction. Evidence showed that in the full trial population, tirzepatide 15 mg was associated with a statistically significantly greater reduction in body weight from baseline compared with placebo (mean percentage change difference -20.1%, 95% confidence interval [CI] -21.2 to -19.0).

Evidence also showed that a statistically significantly larger proportion of people on tirzepatide 15 mg lost 5% or more body weight from baseline (96.3%) compared with placebo (27.9%)

References

1. National Institute for Health and Care Excellence. Technology Appraisal 1026; Tirzepatide for managing overweight and obesity, 23 December 2024. Accessed 31 December 2024.
2. Eli Lilly and Company Limited. Summary of Product Characteristics; Mounjaro KwikPen 2.5mg solution for injection in pre-filled pen, 22 November 2024. Accessed 28 January 2025.
3. NHS Business Services Authority. Dictionary of medicines and devices (dm+d) browser. Accessed 12 December 2024.
4. Medicines and Healthcare products Regulatory Agency. Drug Safety Update; GLP-1 receptor agonists: reminder of the potential side effects and to be aware of the potential for misuse, 24 October 2024. Accessed 28 January 2025.