NHS
Cheshire and Merseyside

TIRZEPATIDE injection (Mounjaro® ▼) for type 2 diabetes

The Cheshire and Merseyside Area Prescribing Group recommends the prescribing of TIRZEPATIDE injection (Mounjaro® ▼), for treating type 2 diabetes in accordance with NICE TA924.

GREEN

Tirzepatide is a first in class dual GLP-1 and GIP receptor agonist which is licensed for the treatment of adults with type 2 diabetes.

NICE technology appraisal (TA) 924 recommends tirzepetide for treating type 2 diabetes alongside diet and exercise in adults when it is insufficiently controlled only if:

- triple therapy with metformin and 2 other oral antidiabetic drugs is ineffective, not tolerated or contraindicated, **and**
- they have a body mass index (BMI) of 35 kg/m^2 or more, and specific psychological or other medical problems associated with obesity, **or**
- they have a BMI of less than 35 kg/m^2, **and**:
  - insulin therapy would have significant occupational implications, or
  - weight loss would benefit other significant obesity-related complications.[1]

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

The NICE committee recommended tirzepatide in line with the company's positioning, that is, as an alternative to GLP-1 receptor agonists in the type 2 diabetes treatment pathway. Current pathways for further management of type 2 diabetes are those described in NICE guideline (NG28) which covers the care and management for adults (aged 18 and over).[2]

The recommendations in NICE TA924 do not extend to use of tirzepetide in combination with insulin, therefore this statement does not recommend use of tirzepetide with insulin.

This statement does not cover the use of tirzepatide for managing overweight and obesity. NICE are currently developing separate guidance for its use for these conditions.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

TIRZEPATIDE injection (Mounjaro® ▼) for type 2 diabetes

Effectiveness

The clinical-effectiveness evidence for tirzepatide came from 4 trials, SURPASS-2 to -5. These were multinational multicentre randomised phase 3 studies. They included assessment of tirzepatide against semaglutide, insulin degludec, insulin glargine and placebo. Other trials (SURMONT trials) were not relevant to this appraisal as they focused on a different indication (weight loss). The committee concluded that tirzepatide (all doses) showed statistically significant reductions in HbA1c and body weight compared with all comparators in SURPASS trials. It also concluded that higher tirzepatide doses gave higher weight reductions. The company highlighted that 81 to 97% of people reached HbA1c levels of less than 53 mmol/mol which was statistically significantly more than with any comparator.[1]

Safety[3]

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) may have an increased risk of hypoglycaemia. The risk of hypoglycaemia may be lowered by a reduction in the dose of the insulin secretagogue.

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 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

Tirzepatide 2.5mg and 5mg KwikPen solution for injection pre-filled syringe x 1 = £92 (cost for 365 days = £1199)

Tirzepatide 7.5mg and 10mg KwikPen solution for injection pre-filled syringe x 1 = £107 (cost for 365 days = £1395)

Tirzepatide 12.5mg and 15mg KwikPen solution for injection pre-filled syringe x 1 = £122 (cost for 365 days = £1590)[4]

Note: The KwikPen contains four doses so one pen provides one month's supply.

Semaglutide 0.25mg, 0.5mg, and 1mg solution for injection pre-filled syringe x 1 = £73.25 (cost for 365 days = £955).[4]

The NICE Resource Impact Template estimates the impact of implementing TA924 to be 13,000 per 100,00 population in 2023/24, £39,000 per 100,000 population in 2024/25, £61,000 per 100,000 population in 2024/25 and £62,000 per 100,00 population in 2025/26 when it is assumed that steady state has been reached.

Patient factors[3]

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 severe renal impairment and ESRD, and severe hepatic impairment is limited, and caution should be exercised.

Paediatric population: The safety and efficacy of tirzepatide in children aged less than 18 years have not yet been established. No data are available.

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 patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines.

Prescribing information[3]

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.

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.

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. When tirzepatide is added to existing therapy of a sulphonylurea, a reduction in the dose of sulphonylurea may be considered to reduce the risk of hypoglycaemia.[2]

Tirzepatide is supplied as one multiple-dose pre-filled KwikPen, which contains 0.6ml of solution. 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.[3]

Implementation notes

NICE TA924 positions tirzepatide as an **alternative** to GLP-1 receptor agonists. The current positioning of GLP-1 receptor antagonists in patients fitting the specified criteria is as follows: if triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, consider triple therapy by switching one drug for a GLP-1 mimetic.[2] Tirzepetide should not be used in addition to a GLP-1 receptor agonist.

The recommendations in NICE TA924 do not extend to use of tirzepetide in combination with insulin, therefore this statement does not recommend use of tirzepetide with insulin.

References

1. National Institute for Health and Care Excellence. Technology Appraisal 924; Tirzepatide for treating type 2 diabetes, 25 October 2023. Accessed 10 November 2023.
2. National Institute for Health and Care Excellence. NICE guideline. Type 2 diabetes in adults: management [NG28]. Published: 02 December 2015 Last updated: 29 June 2022. Accessed online on 22.9.23.
3. Eli Lilly and Company Limited. Summary of Product Characteristics: Mounjaro KwikPen 5mg solution for injection in pre-filled pen. Last updated on emc: 25 March 2024. Accessed online 09 May 2024.
4. NHS Business Services Authority. Dictionary of medicines and devices (dm+d) browser. Accessed 16 November 2023.