NHS
South West London

Dual GIP (glucose-dependent insulinotropic polypeptide)/GLP-1 (Glucagon-like peptide-1) receptor agonist - Tirzepatide (Mounjaro®)

Prescribing considerations

- Should only be initiated by clinicians who are adequately trained and competent to provide training for patients on how to use the injectable device
- See SWL joint formulary for further information regarding formulary choices and prescribing criteria.

Indication

Tirzepatide is recommended 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/m2 or more, and specific psychological or other medical problems associated with obesity, or
- they have a BMI of less than 35 kg/m2, and:
  - insulin therapy would have significant occupational implications, or
  - weight loss would benefit other significant obesity-related complications.

Use lower BMI thresholds (usually reduced by 2.5 kg/m2) for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean family backgrounds.

Mechanism of action

Tirzepatide is a long-acting dual GIP and GLP-1 receptor agonist. Both receptors are present on the pancreatic α and β endocrine cells, heart, vasculature, immune cells (leukocytes), gut and kidney. GIP receptors are also present on adipocytes.

Tirzepatide lowers body weight and body fat mass and improves insulin sensitivity and glycaemic control.

Treatment

Tirzepatide (Mounjaro®):

Dose titration:

Patients should be started on 2.5mg once a week for 4 weeks initially, and then increased to 5mg once a week for at least 4 weeks. (Long-acting injection, which takes approximately 4 weeks to reach steady state).

Thereafter, the dose can be increased, only if necessary/clinically indicated to achieve individual patients' treatment goals, up to a maximum dose of 15mg once a week (depending upon glucose control).

Doses should be increased/titrated in steps of 2.5mg at intervals of at least 4 weeks.

The recommended maintenance doses are 5mg, 10mg and 15mg once a week (7.5mg and 12.5mg doses are available for slower titration).

Missed dosing advice:
If a dose is more than 4 days late, the missed dose should be omitted and the next dose administered at the normal time.

Delivery device:
Tirzepatide is available in doses of 2.5mg, 5mg, 7.5mg, 10mg, 12.5mg and 15mg. Currently only available in the UK in the pre-filled disposable injection device (KwikPen®). Each KwikPen® device contains 2.4ml of solution (0.6ml per dose) and contains 4 doses of each specified strength. The KwikPen® packs do not contain needles. Prescribe screw -on pen needles for the pre-filled device separately.

Cardiovascular (CV) benefit:
The safety and efficacy of tirzepatide was evaluated in five global randomised, controlled, phase 3 studies (SURPASS 1-5) assessing glycaemic control as the primary objective. The studies involved 6 263 treated patients with type 2 diabetes (4 199 treated with tirzepatide). The secondary objectives included body weight, fasting serum glucose (FSG) and proportion of patients reaching target HbA1c.

Tirzepatide SmPC – SURPASS 1-5

Mounjaro does NOT have the evidence of cardiovascular (CV) benefit (superiority for CV endpoints) these studies are ongoing.

Contraindications (Individual product license contains full list)

- Hypersensitivity to the active substance or to any of the excipients (see SPC for full details).

Cautions (Individual product license contains full list)

- Pancreatitis: used with caution in patients with a history of pancreatitis. Acute pancreatitis has been reported in patients treated with tirzepatide. Patients should be informed of the symptoms of acute pancreatitis. If pancreatitis is suspected, tirzepatide should be discontinued.
- Gastrointestinal adverse reactions, which include nausea, vomiting, and diarrhoea have been reported with use. This may lead to dehydration which could lead to a deterioration in renal function including acute renal failure. Advise patients of potential risk of dehydration taking precautions to avoid fluid depletion and electrolyte imbalances.
- Severe gastrointestinal disease, including severe gastroparesis.
- Proliferative/non-proliferative diabetic retinopathy or diabetic macular oedema – appropriate monitoring is recommended.
- Patients aged 85 years or over.

Monitoring & Continuation Criteria

- Similar to GLP-1 mimetic therapy only continue therapy if the adult with T2DM has had a beneficial metabolic response (a reduction of at least 11 mmol/mol [1.0%] in HbA1c and weight loss of at least 3% of initial body weight) in 6 months.
- At each review, check compliance, injection technique, injection site and discuss any possible side effects.

Tirzepatide and insulin

This combination is Amber 2 on the SWL Joint Formulary: initiation by a specialist, stabilisation (approximately three months), then continuation in primary care under an individual management plan.

MHRA/Safety alerts

GLP-1 receptor agonists: reminder of the potential side effects and to be aware of the potential for misuse (October 2024)

Noteworthy Interactions

- If a patient is already on insulin or a sulphonylurea, the dose of either of these may need to be reduced to reduce the risk of hypoglycaemic events when used in combination with tirzepatide (advise patients to take precautions to avoid hypoglycaemia while driving and using machines). Blood glucose self-monitoring is necessary to adjust the dose of sulphonylureas and insulin. A stepwise approach to insulin reduction is recommended. If a patient is using continuous blood glucose monitoring (CGM), agree target HbA1c with the patient and pre-meal blood glucose target levels in line with this HbA1c, and set an alarm for if readings are below this level. Where readings do fall below this, dose changes (reductions) in sulphonylurea or insulin will be needed.
- If a patient is already on metformin and/or sodium-glucose co-transporter 2 inhibitor (SGLT2i) therapy, the current dose of metformin and/or SGLT2i can be continued.
- Patients already on a GLP-1 RA or a DPP-4 inhibitor should have these treatments stopped before starting tirzepatide, as they work on the same pathway or there is therapeutic duplication. Co-prescribing a gliptin with a GLP-1 mimetic is not recommended as both work through the same (incretin) pathway.
- Tirzepatide delays gastric emptying and therefore has the potential to affect the rate of absorption of concomitantly administered oral medicines. This should be considered for oral medicines for which a rapid onset of effect is of importance. No dose adjustments are expected to be required for most concomitantly administered oral medicines. However, it is recommended to monitor patients on oral medicines with a narrow therapeutic index (e.g. warfarin, digoxin), especially during initiation of tirzepatide and following any dose increases
- Refer to individual product license for full list.

Information on adverse effects

- Acute pancreatitis (uncommon): advise the person to seek urgent medical advice if symptoms such as severe upper abdominal pain, nausea, and/or vomiting develop. Advise to discontinue treatment if pancreatitis is suspected

- Alopecia, asthenia, dizziness, hypersensitivity, hypotension, lethargy, malaise, Weight decrease, gallbladder disorders and angioedema.
- Gastrointestinal: decreased appetite, burping, constipation, diarrhoea, gastrointestinal discomfort and disorders, nausea and vomiting.
- Refer to individual product license for full list.

Sick Day rules

If taken during an acute illness that can lead to dehydration, there is an increased risk of developing serious side-effects and therefore should be temporarily stopped. Further information can be found in the sick day rules section.

Disposal

Needles should be disposed of in a sharps bin, which can be prescribed. The full bins can usually be collected by the local council.

Links to local borough sharps disposal information:

- Croydon
- Kingston
- Merton
- Richmond
- Sutton
- Wandsworth

After removing the needle, patients should discard the used KwikPen in household waste or a sharps disposal container.

References

- BNF online (Last accessed 12/11/2024)
- Tirzepatide (Mounjaro®) Factsheet, Medicines Optimisation Team, NHS Kent and Medway (Last accessed 08/09/2022)
- Tirzepatide (Mounjaro®) for treating type 2 diabetes (T2DM) in adults. Prescribing Support Information for Primary Care (Last accessed 08/09/2022)
- SPCs for individual products (Last accessed 12/11/2024)
- SWL Joint Medicines Formulary (Last accessed 12/11/2024)
- Overview | Tirzepatide for treating type 2 diabetes | Guidance | NICE (Last accessed 12/11/2024)

Document History

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