NHS
Kent and Medway

Tirzepatide (Mounjaro®) Factsheet

Mechanism of Action

Tirzepatide (Mounjaro®) is a long-acting dual **GIP/GLP-1 RA** (glucose-dependent insulinotropic polypeptide (**GIP**) receptor and glucagon-like peptide-1 receptor agonist (**GLP-1 RA**), a **new class of medicine**, which increases insulin sensitivity and secretion, suppresses glucagon secretion, and slows gastric emptying. GLP-1 RAs are already well used in the management of type 2 diabetes, while the dual action on the GIP receptor is a new mechanism of action.

Recommended Use

As per NICE TA 924, tirzepatide (Mounjaro®) is recommended for treating type 2 diabetes alongside diet and exercise in **adults (>18 years)** when it is insufficiently controlled, **only if:**

- triple therapy with metformin and two 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.

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 family backgrounds.

Tirzepatide (Mounjaro®) must only be prescribed for the treatment type 2 diabetes in adults. Prescribing outside of this is not supported in Kent and Medway. Prescribing off-label solely for weight loss (in the absence of a type 2 diabetes diagnosis) is not clinically supported or funded by Kent and Medway ICB currently, until NICE have evaluated its use for this indication.

(The safety and efficacy of tirzepatide (Mounjaro®) in children aged <18 years have not yet been established. No data available.)

Across Kent and Medway, the formulary recommendations for GLP-1 RAs are focused on positive **cardiovascular outcomes**. Tirzepatide (Mounjaro®) (dual GIP/GLP-1 RA) does not have this data currently (data is expected in 2025). This should be considered if considering initiating or switching patients to tirzepatide (Mounjaro®).

Formulary Status

Specialist initiation where primary care can initiate, with specialist (in relation to prescribing tirzepatide (Mounjaro®) in Kent and Medway) defined as secondary care prescribers, GPs, Diabetes Specialist Nurses, and specialist pharmacists or nurses (e.g., practice or spoke practice nurses) in primary care who have completed PITstop training or equivalent.

Prescribing Responsibilities

Mounjaro can be initiated in primary care (GPs, Specialist DSNs, and specialist pharmacists or nurses in primary care (e.g. practice or spoke nurses) who have completed PITstop or equivalent).

If is started in another clinic (eg by consultant or trust) then

- The **first 4-week supply** of the 2.5mg dose is to be prescribed by the specialist with a request to primary care to take on the ongoing prescribing of the 5mg dose.
- Upon request to take on prescribing in primary care, it should be made clear that 5mg is the maintenance dose. Apart from clinical exceptions, the initial 2.5mg dose forms part of titration and should not be prescribed on an ongoing/repeat basis (see Dosing & Administration section below).

Formulation/Device

- Tirzepatide is commercially available in the UK under the brand name Mounjaro®. Please **prescribe by brand** (Mounjaro®).
- The **multi-dose** Mounjaro® solution for injection disposable **KwikPen®** is the only device/formulation currently available in the UK. For further clinical information on the KwikPen®, please see the SmPC. Please ensure patients have been counselled on the use of the KwikPen device.
- Please note that the KwikPen® pack(s) **do not contain needles**. **Screw-on needles for pen injectors (4mm) and sharps bin need to be prescribed separately.** If patients are not already prescribed needles (for use with other devices), please issue an acute prescription for **one pack of 100 needles** (which will last >2 years). Please see Guidance on insulin pen needles and preferred formulary choices for Kent & Medway.

Dosing & Administration

Tirzepatide (Mounjaro®) is **administered** by subcutaneous injection **once a week**. *The Mounjaro®▼ KwikPen® (pre-filled pen) contains **4 doses**, therefore **one pen = 4 weeks/28 days' supply***. Please check quantity prescribed.

Dosing:

- 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).

Tirzepatide (Mounjaro®) solution for injection is available in the following **four-dose pre-filled pens (KwikPens®)**:

Strength	Cost per KwikPen® (4-week supply)
2.5mg/0.6ml KwikPen®	£92
5mg/0.6ml KwikPen®	£92
7.5mg/0.6ml KwikPen®	£107
10mg/0.6ml KwikPen®	£107
12.5mg/0.6ml KwikPen®	£122
15mg/0.6ml KwikPen®	£122

- The weekly dose can be administered at **any time of the day**, **with or without meals**. The **day of administration** can be changed if required if the time between two doses is **at least 3 days**.
- Patients and/or their carers must be **counselled** on good injection technique and administration. Tirzepatide (Mounjaro®) is administered via **subcutaneous injection,** into the abdomen, thigh, or upper arm. Injection sites should be rotated with each dose. If a patient also injects insulin, they should inject tirzepatide into a different site.
- Each KwikPen® **dials one specified dose** (designated by a 1 on the dial and the dose can be seen on the label and is colour co-ordinated) and allows priming of the KwikPen® using an 'air-shot', which is two clicks from 0 on the dial and designated by an extended line (-).
- If a **dose is missed**, it should be administered as soon as possible within 4 days after the missed dose. If a dose is more than 4 days late, the missed dose should be omitted and the next dose administered at the normal time. In each case, patients can then resume their regular once weekly dosing schedule.
- No dose adjustment is required based on **age, body weight, gender, race, or ethnicity**.
- No dose adjustment is required for patients with **renal impairment**, including end stage renal disease (ESRD). Experience with the use of tirzepatide (Mounjaro®) in patients with severe renal impairment and ESRD is limited; caution is required.
- No dose adjustment is required for patients with **hepatic impairment**. Experience with the use of tirzepatide (Mounjaro®) in patients with severe hepatic impairment is limited; caution is required.
- The manufacturer recommends **swabbing the KwikPen® prior to use**. This is not universally recommended or commonly part of injection education for other non-insulin and insulin injectable pen devices. If there is a wish to follow the device user manual, please ensure an **alcohol swab** is advised, and note that these **cannot be provided on prescription**.

Concomitant Medication

- 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 (Mounjaro®) (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 (Mounjaro®), as they work on the same pathway or there is therapeutic duplication.
- Tirzepatide (Mounjaro®) 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.

Adverse Effects

- Common side effects include **gastrointestinal side effects** such as nausea, vomiting, diarrhoea and reflux symptoms (similar to the side effects of GLP1-RAs), which slow titration of tirzepatide (Mounjaro®) mitigates.
- **Side effect minimisation advice** e.g. respond to feeling of fullness and stop eating rather than clear the plate, reduce portion size, avoid overly fatty/fried foods, maintain adequate fluid intake, symptoms are often mild and transient, and most people are able to continue medication despite initial nausea.
- As a new drug, Mounjaro®▼ (tirzepatide) is subject to additional monitoring, to quickly identify new safety information. Healthcare professionals are asked to **report any suspected adverse reactions** (minor or serious) to the Yellow Card Scheme.

Monitoring & Review

- Measuring metabolic response at the 6-month interval is not mentioned in NICE TA 924 for tirzepatide (Mounjaro®) as is recommended for GLP-1 RAs. This was mentioned in the committee discussion and was a deliberate omission. However, to reduce the risk of treatment inertia and follow, management of diabetes as per NICE guidance should still be followed. If a patient is not meeting their treatment targets, a review of the medication should be conducted and stopped if clinically indicated/necessary. NICE recommend in NG 28 to measure Hba1c every 3 to 6 months (tailored to individual needs) until HbA1c is stable on unchanging therapy.

Patient Safety, Cautions & Contraindications

- As per the SmPC, when using tirzepatide (Mounjaro®) in **women with obesity or overweight who are using oral contraceptives**, it is advised to switch to a non-oral contraceptive method, or add a barrier method of contraception (e.g., a condom) upon initiating tirzepatide for 4 weeks, and for 4 weeks after each dose increase (as reduced efficacy of oral contraceptives with tirzepatide cannot be excluded). No dose adjustment of oral contraceptives is required in women with normal BMI.
- MHRA advice on GLP-1 receptor agonists: reports of diabetic ketoacidosis (DKA) when concomitant insulin was rapidly reduced or discontinued (June 2019). This is not mentioned in NICE TA 924 for tirzepatide (Mounjaro®), but due to mechanism of action this should be acknowledged.
- Avoid in **pregnancy** and in **women of childbearing potential not using contraception**. If a patient wishes to become pregnant, tirzepatide (Mounjaro®) should be discontinued at least 1 month before a planned pregnancy, due to the long half-life of tirzepatide.
- Use in caution in **breast feeding.** It is unknown whether tirzepatide (Mounjaro®) is excreted in human milk, therefore a risk to the newborn/infant cannot be excluded.
- Patients and/or their carers should be informed how to recognise signs and symptoms of **acute pancreatitis** and advised to seek immediate medical attention if symptoms develop (e.g. severe and persistent abdominal pain, nausea, or vomiting). If pancreatitis is suspected, tirzepatide (Mounjaro®) should be discontinued. If the diagnosis of pancreatitis is confirmed, tirzepatide should not be restarted.
- Patients and/or their carers should be informed of the potential risk of **dehydration** due to gastrointestinal side effects of tirzepatide (Mounjaro®) (nausea, vomiting, diarrhoea) and advised to take precautions to avoid fluid depletion and electrolyte disturbances (particularly elderly patients who may be more susceptible). Dehydration could lead to a deterioration in renal function, including acute renal failure. Ensure sick day guidance given (e.g. ensure adequate fluid intake during acute dehydrating illness and when to seek advice).
- **Contra-indications:** hypersensitivity to the active substance or to any excipients listed in the SmPC.
- **Caution** in patients with severe gastrointestinal disease (including severe gastroparesis).
- **Caution**, and appropriate monitoring, in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy or diabetic macular oedema.
- Mounjaro® contains **benzyl alcohol** (as a preservative), which may cause allergic reactions. Patients with hepatic or renal impairment should be informed of the potential risk of metabolic acidosis due to accumulation over time. See here for questions and answers on benzyl alcohol used as an excipient..

Storage & Disposal

Tirzepatide (Mounjaro®) should be **stored** in a refrigerator (2–8℃) and protected from light by storing in original packaging. In-use Mounjaro® KwikPens® may be stored unrefrigerated at room temperature (not above 30℃) for up to 30 days (and then the KwikPen® must be discarded). Do not freeze.

Each pre-filled KwikPen® contains multiple doses (four doses of 0.6 ml (2.4ml) which can be administered of the total 3ml of solution). The KwikPen®, with any excess solution in after use, should be **disposed** of accordingly.

Further Information & Resources

This factsheet is a summary of the key points/information on tirzepatide (not exhaustive). For more information on tirzepatide (Mounjaro®) including special warnings and precautions for use, side effects/adverse reactions etc., please see the BNF drug monograph for tirzepatide and the SmPC.

This factsheet is to be used in conjunction with the NICE TA on tirzepatide (Mounjaro®) for type 2 diabetes and the NICE guideline on the management of type 2 diabetes in adults.