GLP-1/GIP rollout in Primary Care for managing people living with obesity: what do we know so far?

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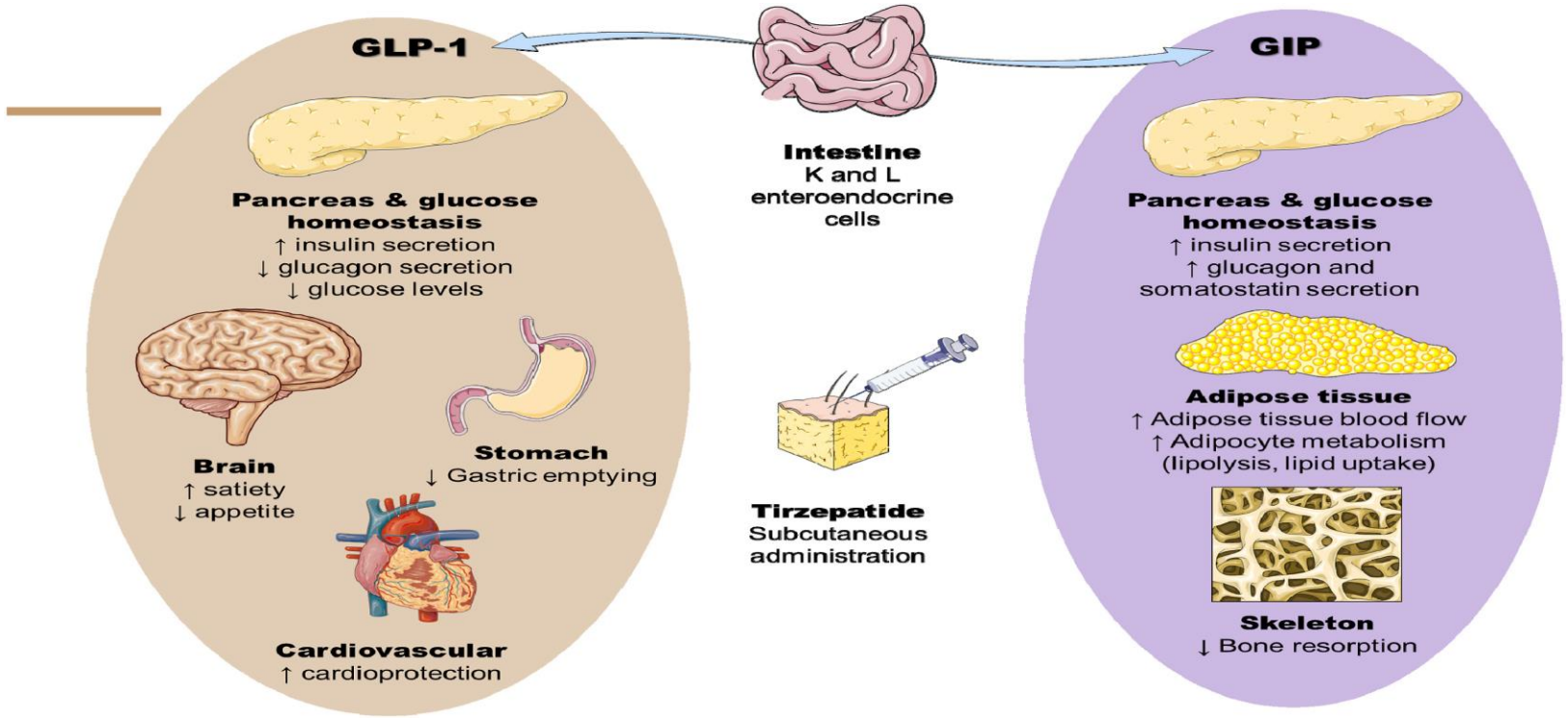
What are GLP-1/ GIP Incretins

- Tirzepatide is a single molecule combining dual agonism of glucose-dependent insulinotropic polypetide (GIP) and glucagon like peptide (GLP-1) receptors agonists, which is administered once weekly.
- GLP-1, secreted by the enteroendocrine L-cells, along with GIP, which is secreted by the enteroendocrine K-cells, are the major determinants of the incretin effect.
- The incretin effect is the enhancement of glucose-dependent insulin secretion from pancreatic beta cells following nutrient ingestion.
- GLP-1 and GIP exert pleiotropic physiological actions, including enhancement of insulin secretion, glyceamic, appetite control, cardio-protection, and adipose tissue improved functions.

Major phsyiological roles of of GLP-1 and GIP

The catcher in the gut: Tirzepatide, a dual incretin analog for the treatment of type 2 diabetes mellitus and obesity - ScienceDirect



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Clinical Evidence

Surmount-1 Trial

Tirzepatide Once Weekly for the Treatment of Obesity | New England Journal of Medicine

- Randomised, double blind trial.
- Compared tirzepatide with placebo, both alongside diet and exercise support – participants were supported by a Dietitian for the full 72 weeks.
- Inclusion: adult with obesity (BMI of 30kg/m2 or more) with or without a comorbidity or overweight (BMI of 27kg/m2 to 29.9kg/m2) with at least one of the following weight related comorbities: hypertension, dyslipideamia, obstructive sleep apnoea or cardiovascular disease, pre-diabetes.
- People with type 2 Diabetes, unstable major depressive disorder or other severe psychiatric disorders within the last 2 years were excluded.
- Trial done in 9 countries, no study site in the UK – but funding has been secured to start the SURMOUNT-UK trial in Manchester.
- Results: show a 94% reduction in risk of progression to type 2 diabetes across all pooled doses of tirzepatide compared to placebo over three years.
- Participants treated with tirzepatide had an average weight reduction of 22.9% (15mg dose).

SURMOUNT-4

Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial | Cardiology | JAMA | JAMA Network

- 36 week of open label maximum tolerated dose of tirzepatide (10 or 15mg), adults (n-670) with obesity or overweight (without diabetes).
- Experienced a mean weight reduction of 20.9%.
- For randomization (at week 36), those switched to placebo experienced a 14% weight regain.
- Those continuing tirzpatide experienced an additional 5.5% weight reduction during the 52- week double blind period.
- Conclusion: Participants with obesity/ overweight, withdrawing tirzepatide led to substantial regain of lost weight, whereas continued treatment maintained and augmented initial weight reduction.

- Aronne LJ, Sattar N, Horn DB, et al. Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial. *JAMA*. 2024;331(1):38–48. doi:10.1001/jama.2023.24945

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NICE recommendations

NICE Recommendations:
NICE Guidance for Tirzepatide

Overview | Tirzepatide for managing overweight and obesity | Guidance | NICE

Published 23 December 2024

- Tirzepatide has been approved to be used in both primary care or a specialist weight management service.
- Recommendation that NHS service providers make tirzepatide available for managing overweight and obesity alongside a reduced calorie diet and increased physical activity.
- It is recommended for adults with a BMI at least 35kg.m2,and with at least one weight related comorbidity.

Phased implementation period

NHS service providers will be required to make tirzepatide available as follows:

- Within 90 days of the guidance's publication, for patients already receiving treatment in specialist weight management services.
- Within 180 days for the guidance's publication, for a further cohort of high–priority patients (with eligibility to be determined by NHS England).
- NICE expects that, at the end of the three- year period around 220 000 patients would have become eligible for treatment.
- Within 12 years of the guidance's publication, for the remainder of patients.

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Prioritisation and Review

- Proposed prioritising patients according to BMI and the number of qualifying comorbidities.
- NICE recommends a modified approach to clinical prioritisations of the eligible population that is more closely aligned with expert opinion.
- NICE will conduct a formal review to be completed within 3 years from the date of final guidance publication.
- It is not NICE's role to specify service delivery models, which is left to NHS England and the ICBs.

Funding Variation Request

- NHS England submitted a funding variation request, on behalf of NHS providers and ICBs, to extend the time needed to comply with the recommendations.

Funding variation allows the following:

- Availability of services
- Clinical capacity
- Inequity of access
- Budget impact

Funding Variation

- NHSE, in conjunction with Integrated Care Boards (ICBs), is proposing an alternative implementation proposal (IP) that would allow for the steady and consistent expansion of service capacity to deliver a tirzepatide treatment pathways aligned to the treatment model.
- Clinical prioritisation for tirzepatide, informed by clinical expertise, begins with the highest clinical need, like the Surmount trial criteria.
- The IP aids the commissioners on how to introduce tirzepatide, setting targets based on the demographic data of the clinical cohorts and commencement is based on capacity.

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Suggested implementation proposal

EXAMPLE:

Cohort 1- approximately 18 months, BMI>40 with >3 qualifying comorbidities

Cohort 2 – approximately 12 months, BMI>40 with 2 qualifying comorbidities

Cohort 3 – approximately 14 months, BMI>40 with 2 qualifying comorbidities (incl. T2DM)

Continues until Cohort 7 which will cover the 12 years proposed programme.

Phased implementation

- Awaiting word from NHSE and ICBS in April with regards to the roll out.
- Contact your local ICB teams

Tirzepatide for managing overweight and obesity - BLUE NWICB are committed to fund positive NICE TA treatments. Awaiting clarification of place in pathway and commissioning arrangements. Further guidance will be issued when available

On 8th November 2023, the Medicines and Healthcare products Regulatory Agency (MHRA) authorised a new indication for Tirzepatide - **weight loss and weight management in adults aged 18 and over.** The medicine is to be used together with a reduced-calorie diet and increased physical activity.

NICE TA1026 was published on 23rd December 2024. Local commissioning arrangements are currently being considered. **Until commissioning is confirmed, there should be no prescribing of Tirzepatide in primary or secondary care for weight management.**

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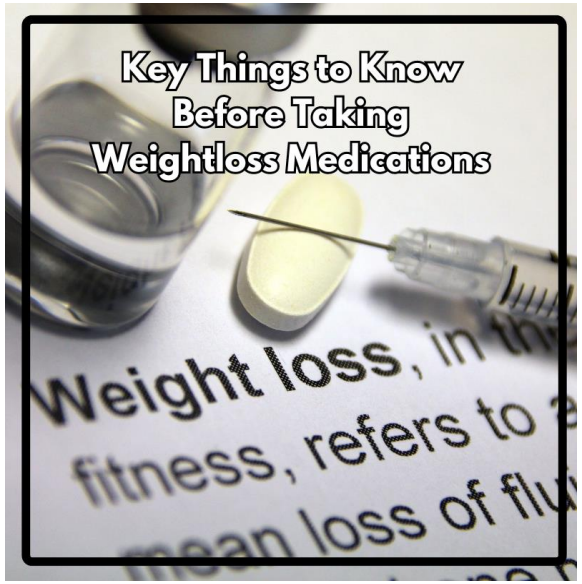
Practical resources when discussing the GLP-1/GIP incretins

Topics that can be discussed in a consultation

- NICE initial assessment checklist
- NICE counselling checklist
- NICE follow up checklist
- Allergies, drug interactions
- Personalised summary
- Medscape resource
- Do they meet the criteria according to NICE
- Side effect and safety netting
- MHRA warning guidance
- Injection – signposting
- Safe disposal of syringes
- Nutritional and behavioural changes

[Tools and resources | Tirzepatide for managing overweight and obesity | Guidance | NICE]



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My personal reference: created for the GP practices at my PCN

Tirzepatide (Mounjaro®) Initially 2.5 mg once weekly for 4 weeks, then increased to 5 mg once weekly for at least 4 weeks, then increased if necessary up to 15 mg once weekly, dose to be increased in steps of 2.5 mg at intervals of at least 4 weeks. .	Tirzepatide has not been approved yet for obesity management on the NHS – it is currently being assessed by NICE. Recommended alongside a reduced-calorie diet and increased physical activity in adults: • BMI of 30kg/m2 or more • Individuals with a BMI of 27kg/m2 with at least one or more weight-related co-morbidity **Discontinue use:** Assess benefit of continuing treatment if at least 5% of initial body-weight has not been lost after 6 months at highest tolerated dose. Potentially available in Primary Care in 2025	Long-acting GIP (glucose-dependent insulinotropic polypeptide) receptor and GLP-1 (glucagon-like peptide-1) receptor agonist that increases insulin sensitivity and secretion, suppresses glucagon secretion, and slows gastric emptying Tirzepatide | Drugs | BNF | NICE **Side Effects:** Alopecia; appetite decreased (in patients with type 2 diabetes); asthenia; burping; constipation; diarrhoea; dizziness; gastrointestinal discomfort; gastrointestinal disorders; hypersensitivity; hypotension; lethargy; malaise; nausea; vomiting	https://onlinedoctor.superdrug.com Starting from £215 **www. https://medexpress.co.uk** **Starting from £149.99** https://onlinedoctor.boots.com Starting from £219 Https://onlinedoctor.lloydspharmacy.com Starting from £169 www. https://onlinedoctor.asda.com Starting from £179

Resources – Medscape Primary Care Hack

https://img.medscapestatic.com/vim/live/professional_assets/medscape/prof_documents/Incretins_Hack_Feb_25_v10.pdf

Use of Liraglutide, Semaglutide, and Tirzepatide for Adults Living With Overweight and Obesity

Medscape UK × Guidelines
Primary Care Hacks

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Incretin Therapy	Indication	Standard Dose Escalation Schedule (in Weeks)									Further Considerations (see also *Prescribing Considerations and Special Precautions for Use*)
		1	2	3	4	5–8	9–12	13–16	17–20	21–24	
Liraglutide (Saxenda®)[3,4]	Weight management, as an adjunct to a reduced-calorie diet and increased physical activity in adults with an initial BMI of: • ≥30 kg/m², or • 27–30 kg/m² in the presence of ≥1 weight-related comorbidity.[A,L,B]	0.6 mg (od)[C]	1.2 mg (od)[C]	1.8 mg (od)[C]	2.4 mg (od)[C]	3.0 mg (od)[C]					• No dose adjustment is required according to age, but therapeutic experience is limited in patients aged ≥75 years and use is not recommended in these patients • No dose adjustment is required in mild/moderate renal impairment (CrCl ≥30 ml/min) or mild/moderate hepatic impairment • Avoid in severe renal impairment (CrCl <30 ml/min), including ESRD • Not recommended in patients with severe hepatic impairment; should be used cautiously in mild/moderate hepatic impairment.
Semaglutide (Wegovy®▼)[5–8]	Weight management, as an adjunct to a reduced-calorie diet and increased physical activity in adults with an initial BMI of: • ≥30 kg/m², or • 27–30 kg/m² in the presence of ≥1 weight-related comorbidity.[A,L,D] To reduce the risk of major adverse CV events in adults with established CVD and BMI ≥27 kg/m²,[A] as an adjunct to a reduced-calorie diet and increased physical activity.	0.25 mg (once weekly)				0.5 mg (once weekly)	1.0 mg (once weekly)	1.7 mg (once weekly)	2.4 mg (once weekly)[E]		• No dose adjustment is required according to age, but there is limited therapeutic experience in patients aged ≥85 years • No dose adjustment is required in mild/moderate/severe renal impairment; avoid in ESRD (eGFR <15 ml/min/1.73 m²) • No dose adjustment is required in hepatic impairment; exercise caution when prescribing in severe hepatic impairment.
Tirzepatide (Mounjaro®▼)[9,10]	Weight management, as an adjunct to a reduced-calorie diet and increased physical activity in adults with an initial BMI of: • ≥30 kg/m², or • 27–30 kg/m² in the presence of ≥1 weight-related comorbidity.[A,L,F]	2.5 mg (once weekly)				5 mg (once weekly)	7.5 mg (once weekly)[G]	10 mg (once weekly)[G]	12.5 mg (once weekly)[G]	15 mg (once weekly)[G]	• No dose adjustment is required according to age, but there are limited data available for patients aged ≥85 years • No dose adjustment is required in renal impairment (including ESRD) • No dose adjustment is required in hepatic impairment; exercise caution when prescribing in severe hepatic impairment.

Footnotes

[A] **NICE recommends lower BMI thresholds (usually, reduced by 2.5 kg/m²) for people of South Asian, Chinese, other Asian, Middle Eastern, Black African, or African–Caribbean family backgrounds**[4,7,10]

[B] NICE TA664[4] recommends liraglutide for overweight or obesity if it is prescribed by a specialist, multidisciplinary, tier-3 weight-management service and is provided according to the commercial arrangement for the drug. NICE recommends provision in patients with all of the following: a BMI of ≥35 kg/m²; nondiabetic hyperglycaemia (HbA1c of 42–47 mmol/mol or fasting plasma glucose of 5.5–6.9 mmol/l); and high risk of CVD, based on risk factors.[A] After 12 weeks of treatment with the 3.0 mg/day dose, treatment should be discontinued if patients have not lost ≥5% of their initial bodyweight[3]

[C] If escalation to the next dose is not tolerated for 2 weeks consecutively, consider discontinuing treatment[3]

[D] NICE TA875[7] recommends semaglutide if it is used for a maximum of 2 years, is prescribed within a specialist weight-management service providing multidisciplinary management, and is provided according to the commercial arrangement for the drug; NICE recommends provision in patients with ≥1 weight-related comorbidity and either a BMI ≥35 kg/m² or a BMI of 30–34.9 kg/m² if the patient meets the criteria for referral to specialist weight-management services in NICE NG246;[7,10,A] if weight loss is <5% of initial weight after 6 months of treatment, consider stopping semaglutide;[7] as the SELECT trial has demonstrated CV benefits of semaglutide irrespective of weight loss, it may be worth considering continuation independent of weight loss when used for CV indications[8]

[E] If semaglutide is not tolerated at 2.4 mg, maintain at 1.7 mg for 4 more weeks then re-escalate afterwards[6]

[F] NICE TA1026[10] recommends prescribing tirzepatide for adults with a BMI of ≥35 kg/m² and ≥1 weight-related comorbidity;[A] if weight loss is <5% of initial weight after 6 months of treatment, consider stopping tirzepatide

[G] Individualise tirzepatide above 5 mg depending on individual treatment goals, increasing dose by 2.5 mg after ≥4 weeks at current dose; 5 mg, 10 mg, and 15 mg are the recommended maintenance doses.[9]

This table is based on the authors' interpretation of summaries of product characteristics and relevant guidance. HCPs are asked to report all suspected adverse drug reactions to products with a Black Triangle symbol (▼) through the Yellow Card Scheme: yellowcard.mhra.gov.uk

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For references and to view this Primary Care Hack online, go to **medscape-uk.co/Hack-incretin**

Last updated: February 2025.

Medscape Primary Care Hack

Brand Names of Incretin Therapies for Different Indications[3,5,9,12–15]

Drug	Brand Name (Maximum Dose) for Weight Management	Brand Name (Maximum Dose) for T2D	Notes
Liraglutide	**Saxenda®** (up to 3.0 mg daily)	**Victoza®** (up to 1.8 mg daily)	• Liraglutide is also now available as an authorised generic in US markets (for T2D).[13]
Semaglutide	**Wegovy®▼** (up to 2.4 mg weekly)	**Ozempic®** (up to 2.0 mg weekly)	—
Tirzepatide	**Mounjaro®▼** (up to 15 mg weekly)		• In the UK, tirzepatide is currently only branded as Mounjaro®▼ • In the US, the FDA has approved Mounjaro®▼ for T2D and Zepbound® for weight management.[15]

Practical Considerations—Injection, Storage, Driving[3,5,9]

- Incretin therapies are injected **subcutaneously** in the **abdomen, thigh, or upper arm**
- Needles must be prescribed separately for liraglutide and tirzepatide when used for weight management; 4 mm needles will usually be suitable
- **Injection sites should be rotated**
  - if the individual also injects insulin, they should inject the incretin therapy into a different site
- Do not forget to issue a **sharps bin**—a 1.8-litre bin is usually adequate
- Store incretin therapies in a refrigerator at 2–8°C, away from the cooling element; do not freeze incretin therapies
  - **liraglutide:** after first use, store at <30°C (preferably, at 2–8°C in a refrigerator); pens should be discarded after 30 days, even if they still contain medication
  - **semaglutide:** after first use, store at <30°C (preferably, at 2–8°C in a refrigerator) for up to 6 weeks
  - **tirzepatide:** may be stored unrefrigerated for ≤30 days at <30°C
- **Incretin therapies have a negligible impact on the ability to drive or use machines**
  - however, if using incretin therapies alongside insulin or SUs, the usual advice and precautions should be given to avoid hypoglycaemia when driving or operating machinery. Ensure adherence with DVLA requirements.

Behavioural Modifications and Interventions[3,5,9,11,16–25]

- **Consider recommending behavioural modifications to all people with overweight or obesity**
  - offer a brief intervention to people living with overweight or obesity, using ASK, ASSESS, ADVISE, AGREE, and ASSIST;[19] see also PHE guidance
  - in these discussions, be aware of weight bias, stigma, and how language matters
  - use specific conversation techniques that have been shown to support brief, effective, and well-received conversations about weight loss
- Adequate support of behavioural modifications, as well as mental health care, needs to be considered **during** and **before** incretin therapy initiation
- Consider **multicomponent interventions**, involving behaviour modification strategies and motivational interviewing; key areas to support include:
  - **nutrition** (including eating behaviours and diet content)
  - **increased physical activity** (including maintenance of muscle mass)—discuss the importance of resistance training to aid preservation of muscle mass and function
  - **stress management**
  - **sleep health**
- Set **personalised goals** that are realistic and achievable
  - use a SMART goal-setting framework[23]
- Behavioural modifications should focus on **whole health gain,** not just weight loss, as this approach has been shown to improve long-term weight and behavioural outcomes[24]
- **Be aware that mental illness can impact obesity management efforts;** screen patients for potential mental illnesses that need to be addressed.[25]

Women's Health and Incretin Therapies[3,5,9]

- **Incretin therapies are not recommended during breastfeeding and pregnancy**
  - **women of childbearing potential should use contraception**
- For women planning pregnancy:
  - liraglutide: discontinue before attempting to conceive
  - semaglutide: discontinue ≥2 months before attempting to conceive
  - tirzepatide: discontinue ≥1 month before attempting to conceive
- **Specific OCP advice for tirzepatide:**
  - **women with a normal BMI:** no dose adjustment of OCP is required
  - **women with obesity or overweight:** switch to a non-oral contraceptive method, or add a barrier method of contraception upon initiation or dose escalation of tirzepatide (for 4 weeks).

Side Effects[3,5,6,9,26–31]

- The side effects of incretin therapies can lead to nonadherence and discontinuation—in one study of GLP-1 RA use, 21.2% of people had discontinued therapy by 12 months and only 48.6% were adherent[26]
- **The most common adverse effects (prevalence ≥10%) are mostly GI in nature.** GI side effects mostly occur during dose escalation, usually fade with time, and are typically mild/moderate in severity
  - examples include nausea, vomiting, diarrhoea, constipation, abdominal pain, abdominal distension, dyspepsia, flatulence, and belching
- Hair loss (likely due to telogen effluvium; usually transient and reversible),[27,28] fatigue, headache, dizziness, and a small increase in resting HR (around 3 bpm on average, and not clinically significant) can also commonly occur.

Managing GI Side Effects

- **Incretin therapies should be used with caution in people with severe GI disease**, e.g. severe gastroparesis
- **GI side effects are dose-dependent, so consider slower dose escalation or drug holidays** (temporary cessation of incretin therapy) for those who are struggling with GI side effects in the early weeks of therapy
  - a lower maintenance dose can be considered for individuals unable to tolerate the usual maintenance dose
- Advise patients reporting GI side effects to adopt the following mitigating strategies:
  - eat slowly, stop eating as soon as you start to feel full, and avoid eating when not feeling hungry
  - eat smaller portion sizes and eat more frequently during the day, but avoid eating late in the day
  - maintain good hydration, aiming for ≥2–3 litres of fluids daily (not including alcohol)
    - limit intake of alcohol and fizzy drinks, especially if experiencing nausea or dyspepsia
  - avoid eating high-fat, ultra-processed, and spicy foods
  - increase fibre and water intake if experiencing constipation
  - consider short-term use of PPIs, antiemetics, laxatives, and antidiarrhoeal medications for those with disabling side effects
- Consider alternative causes of GI symptoms if persistent despite mitigation strategies, or if red-flag features are present.

Minimising Occurrence/Severity of GI Adverse Effects: General Guidance[29]

Gorgojo-Martínez J, Mezquita-Raya P, Carretero-Gómez J et al. Clinical recommendations to manage gastrointestinal adverse events in patients treated with glp-1 receptor agonists: a multidisciplinary expert consensus. *J Clin Med* 2022; **12** (1): 145.

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For references and to view this Primary Care Hack online, go to **medscape-uk.co/Hack-incretin**

Last updated: February 2025.

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Advice for Missed Doses[3,5,9,31]

	Day of Usual Administration	Number of Days After Missed Dose					
		Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Semaglutide	Missed dose	Administer catch-up dose as soon as possible (within 5 days)				Skip dose and administer next dose on usual day	
Tirzepatide	Missed dose	Administer catch-up dose as soon as possible (within 4 days)				Skip dose and administer next dose on usual day	

After a dose of semaglutide or tirzepatide is missed (regardless of whether a catch-up dose is taken), individuals can then resume their regular once-weekly dosing schedule.

Note: the time between any two doses must always be ≥72 hours.

	0–12 hours after a missed dose	12–24 hours after a missed dose
Liraglutide	Administer catch-up dose as soon as possible	Skip dose and administer next dose on usual day

If >3 days have elapsed since the last dose, reinitiate liraglutide at 0.6 mg daily and follow the usual dose escalation schedule.[31]

Special Considerations for People With T2D and Overweight/Obesity[3,5,9,12,14,37–41]

- Incretin therapies are **not** currently licensed for use in people with T1D and overweight/obesity
- Deprescribe any DPP4 inhibitor if initiating an incretin therapy
- Based on the findings of a systematic review and meta-analysis, people **without** T2D may achieve significantly greater mean weight loss with GLP-1 RAs than people **with** T2D[37]
- **Risk of hypoglycaemia is low if the incretin therapy is not used alongside insulin or SUs**
  - people with T2D taking insulin or SUs may need to lower the dosage of these medications initially when starting incretin therapies, to reduce the risk of hypoglycaemia
  - SMBG is necessary when adjusting the dose of SU or insulin, and a stepwise approach to insulin reduction is recommended
- **DKA risk**
  - the MHRA (2019)[38] warns of reports of DKA when insulin is rapidly reduced or discontinued alongside GLP-1 RAs
  - any dose reduction of insulin should be done in a stepwise manner, with careful SMBG
- **Retinopathy—be aware that pre-existing DR may be worsened if HbA_{1c} is rapidly lowered on initiation or escalation of incretin therapy**
  - use all incretin therapies with caution in patients who have DR requiring active ophthalmology follow up, suboptimal glycaemic control (HbA_{1c} ≥86 mmol/mol), and are currently being treated with insulin[39–41]
  - ensure that all people living with T2D being considered for incretin therapies are up to date with retinal screening.

Prescribing Considerations[3,5,9,31–36]

- Incretin therapies can be administered at any time of the day, with or without meals
  - injections of semaglutide and tirzepatide should be scheduled on the same day each week, but the time can be varied
  - if a change of day is required for semaglutide or tirzepatide, **the time between the two doses during transition must be ≥3 days (≥72 hours)**
- **All incretin therapies delay gastric emptying and therefore have the potential to impact the absorption of coadministered oral medications;** however, no dose adjustments are required for most oral medications
  - if individuals are taking oral medications with a **narrow therapeutic index** (e.g. digoxin, lithium, warfarin), closer monitoring may be warranted according to clinical judgement
  - **specific OCP advice is required for tirzepatide** (see *Women's Health and Incretin Therapies*)
- **Sick day guidance** may be required:[32,33] during any intercurrent dehydrating illness (e.g. diarrhoea or vomiting), a temporary pause of incretin therapy may be required to avoid worsening of any GI or other symptoms
  - the incretin therapy can be restarted when the patient is eating and drinking as normal and recovered from illness
- Incretin therapies can be used as adjunctive treatment after bariatric surgery for those with suboptimal weight loss or weight regain, offering a viable alternative to revision surgery.[34] However, this approach should be discussed with a specialist in bariatric surgery and medicine
- **Contraindications:**
  - hypersensitivity to the active substance or any of the excipients present in the incretin therapy
  - according to the US SPCs, all incretin therapies are contraindicated in individuals with MEN2 or with a personal or family history of MTC[35]
    - however, a 2023 systematic review and meta-analysis found that **semaglutide use in RCTs and real-world studies was not associated with an increased risk of any types of cancer (including pancreatic and thyroid cancer).**[36]

Special Precautions for Use[3,5,9,42]

Adverse Effect	Frequency	Notes
Acute pancreatitis	≤1% (uncommon)	• Use with caution in people with a history of pancreatitis • Discontinue if pancreatitis is suspected.
Acute gallbladder disease (cholelithiasis, cholecystitis)	≤1% (uncommon)[A]	• Significant or rapid weight loss can increase the risk of gallstones[42] • If gallbladder disease is suspected, consider gallbladder imaging and appropriate clinical follow up as indicated.[42]
Pulmonary aspiration	—	• Cases of pulmonary aspiration have been reported in people undergoing GA or deep sedation who are receiving incretin therapies • Before such procedures, the increased risk of residual gastric content (due to delayed gastric emptying) should be considered • UK societies have developed a consensus statement giving guidance on the perioperative management of incretin therapies: individuals should continue to take their GLP-1 and GIP RAs throughout the perioperative period

[A] Cholelithiasis is listed as a common (≤10%) adverse effect of semaglutide[5] and liraglutide.[31]

Follow Up[3,7,10,11,17,43–49]

- **Provide long-term, multicomponent, multimodal, multidisciplinary follow up to all people living with overweight or obesity**
- **Set personalised goals that:**
  - emphasise long-term, realistic, sustained weight loss
  - promote weight maintenance and prevention, improvement, and resolution of obesity-related diseases, disorders, and complications
- Consider agreeing a realistic 'best weight' (i.e. a weight that a person can achieve and maintain in the context of their life circumstances)[43]
- **Evaluation of response to incretin therapies is crucial:**
  - consider intensification of therapy or additional therapeutic options (e.g. metabolic surgery) if individualised goals are not achieved
  - consider stopping incretin therapies if <5% of the initial weight has been lost after 6 months of the highest tolerated dose of tirzepatide or semaglutide, or after 12 weeks of the highest tolerated dose of liraglutide[3,7,10]
  - ensure appropriate/optimal prescribing; consider deprescribing medications that may no longer be indicated due to the health benefits of weight loss (e.g. antihypertensives)
  - consider reassessing goals of therapy during treatment course
  - long-term use of pharmacotherapy is recommended
- **Explain that regular physical activity is beneficial for weight maintenance** and improves cardiometabolic risk factors, health-related quality of life, and mood disorders[45]
  - in weight management interventions, aerobic and resistance exercise supports improvements in cardiorespiratory fitness, mobility, strength, and **muscle mass**; support strategies to minimise muscle loss
  - resistance training in particular can promote weight maintenance and modest increases in muscle mass
- **Set a defined timescale for follow up**
  - consider regular monitoring, as clinically indicated, to assess obesity and its related diseases, disorders, and complications (consider using the *Type 2 Diabetes CVRM Review Checklist*)
  - remember that managing obesity-related diseases, disorders, and complications is part of obesity management
- **Be aware of the risks of weight cycling on cardiometabolic health and adopt strategies that focus on sustained changes that maintain healthy habits over time**[46,47]
- Be aware that incretin therapies **may increase the risk of mental health disorders and suicidal behaviours.**[48] Assess mental health in all individuals on incretin therapies and manage as clinically indicated.

BMI=body mass index; **bpm**=beats per minute; **CrCl**=creatinine clearance; **CV**=cardiovascular; **CVD**=cardiovascular disease; **CVRM**=cardiovascular–renal–metabolic; **DKA**=diabetic ketoacidosis; **DPP4**=dipeptidyl peptidase-4; **DR**=diabetic retinopathy; **DVLA**=Driver & Vehicle Licensing Agency; **eGFR**=estimated glomerular filtration rate; **ESRD**=end-stage renal disease; **FDA**=Food and Drug Administration; **GA**=general anaesthesia; **GI**=gastrointestinal; **GIP**=glucose-dependent insulinotropic polypeptide; **GLP-1**=glucagon-like peptide-1; **HbA_{1c}**=glycated haemoglobin; **HCP**=healthcare professional; **HR**=heart rate; **LTC**=long-term condition; **MEN2**=multiple endocrine neoplasia type-2; **MHRA**=Medicines and Healthcare products Regulatory Agency; **MTC**=medullary thyroid carcinoma; **NG**=NICE Guideline; **OCP**=oral contraceptive pill; **od**=once daily; **PHE**=Public Health England; **PPI**=proton pump inhibitor; **RA**=receptor agonist; **RCT**=randomised controlled trial; **SMART**=Specific, Measurable, Achievable, Rewarding, Timely; **SMBG**=self-monitoring of blood glucose; **SPC**=summary of product characteristics; **SU**=sulfonylurea; **TA**=Technology Appraisal; **T1D**=type 1 diabetes; **T2D**=type 2 diabetes.

@GLNS_Medscape @drkevinfernando medscape.co.uk/guidelines

For references and to view this Primary Care Hack online, go to **medscape-uk.co/Hack-incretin**

Last updated: February 2025.

Medicines and Healthcare products Regulatory Agency

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

Healthcare professionals are reminded to inform patients about the common and serious side effects associated with glucagon-like peptide-1 receptor agonists (GLP-1RAs).

Advice for healthcare professionals:

- inform patients upon initial prescription and when increasing the dose about the common risk of gastrointestinal side effects which may affect more than 1 in 10 patients. These are usually non-serious, however can sometimes lead to more serious complications such as severe dehydration, resulting in hospitalisation
- be aware that hypoglycaemia can occur in non-diabetic patients using some GLP-1RAs for weight management; ensure patients are aware of the symptoms and signs of hypoglycaemia and know to urgently seek medical advice should they occur
- patients should also be warned of the risk of falsified GLP-1 RA medicines for weight loss if not prescribed by a registered healthcare professional, and be aware that some falsified medicines have been found to contain insulin[1]
- be aware there have been reports of potential misuse of GLP-1RAs for unauthorised indications such as aesthetic weight loss
- report suspected adverse drug reactions to the Yellow Card scheme

Advice for healthcare professionals to provide to patients:

- GLP-1RAs are prescription-only medicines to be used under medical supervision and should only be prescribed by a registered healthcare professional
- the benefits and risks of using a GLP-1RAs for weight loss outside of the licensed indications have not been studied
- common gastrointestinal side-effects of GLP-1RAs treatment (including nausea, vomiting, diarrhoea and constipation) can persist for several days and may affect more than 1 in 10 patients. This may result in dehydration, which if severe may lead to other serious health complications such as kidney damage resulting in hospitalisation
- throughout treatment stay well hydrated by drinking plenty of fluids (such as water) to avoid dehydration, which can sometimes occur after experiencing gastrointestinal side-effects including vomiting and diarrhoea
- other serious but less common side-effects of GLP-1RAs include acute gallstone disease, pancreatitis, and serious allergic reactions
- if obtaining a private prescription (from a non-NHS prescriber), ensure that this is dispensed from authorised sources, such as registered online pharmacies, to avoid the risk of receiving falsified pens
- carefully read the instructions for use in the Patient Information Leaflet, and use the prescribed dose
- if you are concerned about any side-effects, speak to a healthcare professional

Report any suspected adverse drug reactions

Healthcare professionals should continue to report suspected adverse drug reactions to the Yellow Card scheme. When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, product brand name, details of your suspicion of inappropriate use or misuse and include all relevant patient details including weight or BMI, and if possible, where the product was obtained (i.e. NHS prescription, private prescription, including online prescriptions, or illegitimate supplier). Reporting suspected ADRs, even those known to occur, adds to knowledge about the frequency and severity of these reactions and can be used to identify patients who are most at risk. Your report helps the safer use of medicines.

Healthcare professionals, patients, and caregivers are asked to submit reports using the Yellow Card scheme electronically using:

- the Yellow Card website
- the Yellow Card app; download from the Apple App Store or Google Play Store
- some clinical IT systems for healthcare professionals (EMIS, SystmOne, Vision, MiDatabank, and Ulysses

For queries or more information, please contact info@mhra.gov.uk

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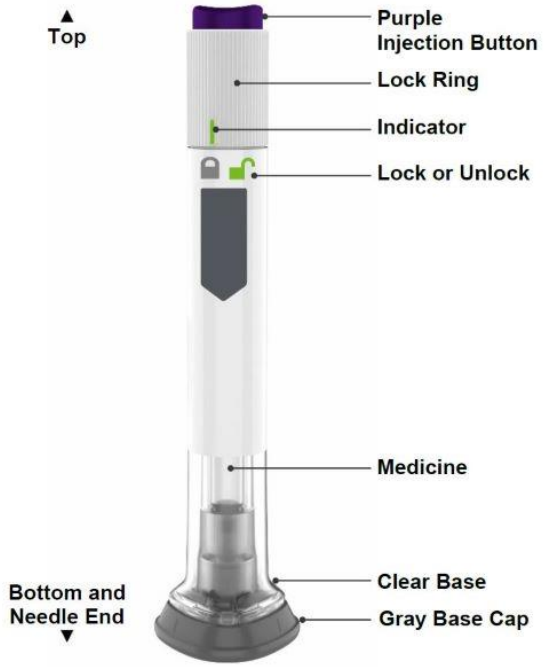
How to Use- Signposting / Discuss if purchasing online what to consider

https://mounjaro.lilly.com/how-to-use-mounjaro

- How to inject and dosing Mounjaro
- How to store the Mounjaro pen
- How to dispose of the Mounjaro pens
- Managing possible side effects and serious side effects

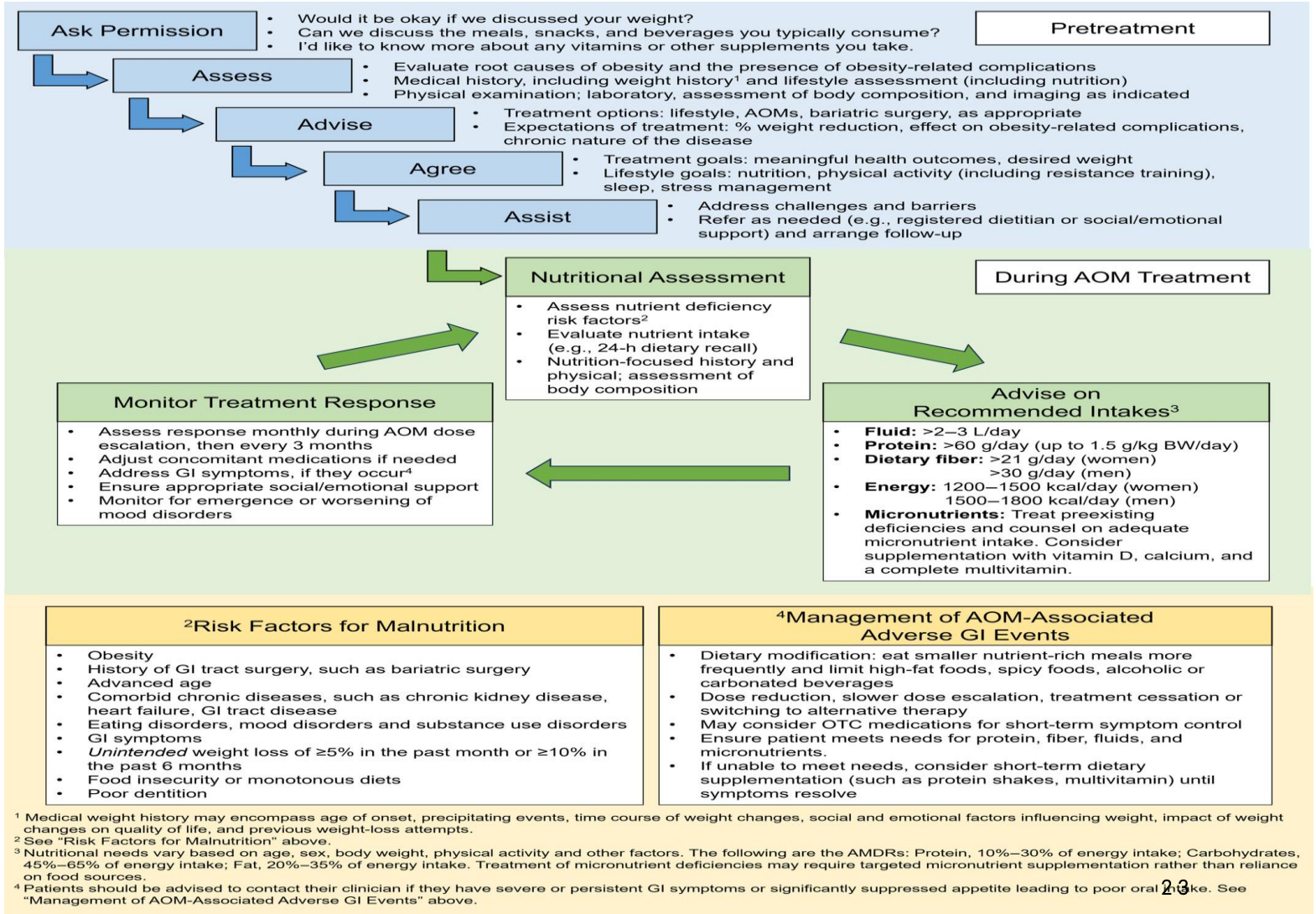


Nutritional Considerations

- Nutritional considerations with antiobesity medications - Almandoz - 2024 - Obesity - Wiley Online Library

- Review which provides practical nutritional recommendations and tips for patient monitoring and management and promote optimal health outcomes

Obesity, Volume: 32, Issue: 9, Pages: 1613-1631, First published: 10 June 2024, DOI: (10.1002/oby.24067)



Thank You

BDA The Association of UK Dietitians

First Contact Dietitians

Specialist Group

References

- NICE technology appraisal guidance. Tirzepatide for Managing overweight and obesity. 23 December 2024.

Overview | Tirzepatide for managing overweight and obesity | Guidance | NICE

- A.Jastreboff; L. Aronne; N.Ahmad; et.al. Tirzepatide Once Weekly for the Treatement of Obesity. The New Engalnd Journal of Medicine. 2022; 287 (3):205-216.

Tirzepatide Once Weekly for the Treatment of Obesity | New England Journal of Medicine

- L. Arrone; N. Sattar; D. Horn; et al. Continued treatment with tirzepatide for maintenancse of weight reduction in adults with obesity: The SURMOUNT-4 Randomized Clinical Trial. JAMA. 2024; 331(1):38-41

Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial | Cardiology | JAMA | JAMA Network

- I.Lempis; J Liu; M. Dalamaga. THe catcher in the gut: Tirzepatide, a dual incretin analog for the treatment of type 2 diabetes mellitus and obesity. Metabolism Open. 2022. 16

The catcher in the gut: Tirzepatide, a dual incretin analog for the treatment of type 2 diabetes mellitus and obesity- ScienceDirect

- J. Almoandoz; T. Wadden; C. Tewksury; et .al. Nutritional considerations with antiobesity medications. Obesity A Research Journal. . 32 (9): 1613-1631.

Nutritional considerations with antiobesity medications - Almandoz - 2024 - Obesity - Wiley Online Library

- Treatment with tirzepatide in adults with pre-diabetes and obesity or overweight resulted in sustained weight loss and nearly 99% remained diabetes-free at 176 weeks | Eli Lilly and Company
- MHRA authorises diabetes drug Mounjaro (tirzepatide) for weight management and weight loss - GOV.UK
- How to Use, Dosing & Side Effects | Mounjaro® (tirzepatide)
- Obesity/Overweight, Adults: Incretin Therapies—Primary Care Hack