Obesity Management & GLP-1 Agents

Who qualifies, how to titrate, what to monitor · and the two guideline reversals residents still get wrong

Treat the disease
not the number

WHO QUALIFIES *and what each tier actually buys*

LIFESTYLE, FOR EVERYONE

Target **5% to 10%** of baseline weight. That range is where blood pressure, glycemia, triglycerides and hepatic steatosis reliably improve, **even if the patient never leaves the obese BMI range**. Counsel on it at least annually.

PHARMACOTHERAPY

BMI ≥ 30, or **BMI ≥ 27 with a weight-related comorbidity** (T2DM, hypertension, dyslipidemia, OSA, MASLD). Add to lifestyle, never instead of it.

METABOLIC / BARIATRIC SURGERY

BMI > 35 regardless of comorbidity, and **consider at BMI 30 to 34.9 with metabolic disease** (ASMBS/IFSO 2022). **This replaced the NIH 1991 criteria** of BMI 40, or 35 with a comorbidity, which are still widely quoted.

BEFORE YOU PRESCRIBE *three things that change the plan, all easy to skip*

EXCLUDE SECONDARY CAUSES

Hypothyroidism (TSH), **Cushing's syndrome** (proximal weakness, striae, easy bruising, new diabetes and hypertension together), **hypothalamic injury**, and **PCOS**. Rare as a whole, but each is treatable and none responds to a GLP-1.

SWAP THE OBESOGENIC DRUG FIRST

Review the list before adding one: **antipsychotics** (olanzapine, clozapine, quetiapine), **insulin and sulfonylureas**, **glucocorticoids**, **mirtazapine and some SSRIs**, **gabapentin and pregabalin**, **beta-blockers**. **Changing the culprit is cheaper and faster than treating the consequence.**

SCREEN THE TRAVELLING COMPANIONS

OSA (STOP-BANG), **MASLD** (FIB-4), **T2DM or prediabetes**, lipids, blood pressure, and **depression**. These are the conditions the weight is driving, and treating them is much of the benefit.

THE AGENTS *titration is slow on purpose: it is how you keep the patient on the drug*

Drug	Dosing and titration	Mean weight loss	Notes
Tirzepatide (Zepbound) GIP + GLP-1	**2.5 mg SC weekly**, then **+2.5 mg every 4 weeks**: 5, 7.5, 10, 12.5, **15 mg**	**~22.5%** at 72 wk SURMOUNT-1	Most effective agent available. Maintenance is 10 or 15 mg, or the maximum tolerated
Semaglutide (Wegovy) GLP-1	**0.25 mg SC weekly**, then every 4 weeks: 0.5, 1.0, 1.7, **2.4 mg**	**~15%** at 68 wk STEP 1	The only agent with a **cardiovascular outcome benefit in obesity without diabetes** (see below)
Liraglutide (Saxenda)	**0.6 mg SC daily**, uptitrate weekly to **3.0 mg**	~8%	Daily injection, now largely superseded, but useful where weekly agents are unavailable
Phentermine / topiramate **Naltrexone / bupropion** **Orlistat**	Oral options	~5 to 10%	Consider when injectables are not accessible or not tolerated. Phentermine/topiramate is **teratogenic**: pregnancy test and contraception. Naltrexone/bupropion is contraindicated with **seizure disorder** or opioid use

BEYOND WEIGHT *why these are cardiometabolic drugs, not cosmetic ones*

Evidence	What it showed, and what it changes
SELECT, 2023 semaglutide 2.4 mg	**17,604 adults with established CVD and overweight or obesity, without diabetes. 20% reduction in MACE** (CV death, nonfatal MI, stroke). The benefit was **largely independent of how much weight was lost**, which is the argument that these are disease-modifying rather than weight drugs. Practical effect: in a patient with ASCVD and obesity but no diabetes, this is now a cardiovascular indication
CKM syndrome framing 2026 AHA/ACC/ADA/ASN	Obesity is **Stage 1**, the first actionable stage, and weight loss is the main lever for **stage regression**. Obesity pharmacotherapy and surgery are added as needed to reach the 5% to 10% target rather than being held in reserve

MONITORING, HARMS & STOPPING

Issue	What to do about it
GI intolerance the usual reason for stopping	Nausea, vomiting, constipation, diarrhea. Nearly always dose-related and worst after each escalation. **Slow the titration or hold at the current dose** rather than abandoning the drug. Small meals, stop eating at satiety
Muscle mass loss	A meaningful fraction of weight lost is lean mass. **Resistance training and adequate protein are part of the prescription**, not optional advice, and this matters most in older and frail patients
Contraindications	**Personal or family history of medullary thyroid carcinoma or MEN2** (class boxed warning). **Stop in pregnancy** and discuss contraception before starting. Caution with prior pancreatitis and with gastroparesis
Gallbladder disease	Rapid weight loss raises gallstone and cholecystitis risk. Consider it in anyone on therapy presenting with right upper quadrant pain
Non-response at 12 weeks	A **12-week checkpoint at the maintenance dose appears in the labeling** for several agents: if weight loss is **under 5%**, do not simply continue. Check adherence and injection technique first, then **switch agent or refer for surgery** rather than waiting another year on a drug that is not working
Stopping the drug	**Weight is regained after discontinuation**, and a large share of it. Frame treatment as **chronic disease management** from the first visit, the way you would antihypertensives, so that stopping is a decision rather than a default

Do not prescribe two of the same molecule. Semaglutide is **Wegovy** for obesity (to 2.4 mg) and **Ozempic** for T2DM (to 2.0 mg); tirzepatide is **Zepbound** for obesity and **Mounjaro** for T2DM. The brand differs by indication and maximum dose, not by drug, so a patient can arrive on both and be double-dosed.

TWO REVERSALS RESIDENTS STILL GET WRONG

- **Perioperative: the blanket hold is out of date.** The 2023 ASA guidance advised holding weekly agents for a week before a procedure. **The December 2024 multi-society guideline replaced that: most patients may continue their GLP-1**, with individualized risk assessment rather than an automatic stop. The underlying concern is delayed gastric emptying and residual gastric contents, so assess GI symptoms and recent dose escalation, and escalate airway precautions if concerned rather than reflexively cancelling.
- **Bariatric surgery thresholds moved in 2022.** BMI **> 35 alone is sufficient**, and 30 to 34.9 with metabolic disease should be considered. Quoting the NIH 1991 numbers (40, or 35 with a comorbidity) **under-refers patients who now qualify**, and surgery still outperforms medication for durable weight loss and diabetes remission.

References: SURMOUNT-1 · STEP 1 · SELECT (NEJM 2023) · 2022 ASMBS/IFSO indications for metabolic and bariatric surgery · 2024 multi-society perioperative GLP-1 guidance · 2026 AHA/ACC/ADA/ASN CKM guideline · FDA prescribing information.

Educational aid; verify against current guidance, local formulary and patient factors.

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