

Effective Weight-Loss Medications (Ranked by Average Weight Loss)

Approximate mean total body weight loss at 1 year+ when combined with lifestyle intervention. Individual response varies considerably.

Rank	Medication	Typical Weight Loss	Dosing Regimen	Common Side Effects	Important Contraindications / Cautions
1	Tirzepatide (Mounjaro)	~15–22%	Start 2.5 mg SC weekly × 4 weeks, then 5 mg weekly. Increase by 2.5 mg every ≥4 weeks to 10–15 mg weekly.	Nausea, vomiting, diarrhoea, constipation, reflux, reduced appetite, gallstones	Personal/family history of medullary thyroid carcinoma (MTC), MEN2, pregnancy
2	Semaglutide (Wegovy)	~10–15%	Start 0.25 mg SC weekly. Escalate every 4 weeks: 0.5 → 1.0 → 1.7 → 2.4 mg weekly.	Nausea, vomiting, diarrhoea, constipation, delayed gastric emptying	MTC/MEN2, pregnancy, caution with severe gastroparesis
3	Liraglutide (Saxenda)	~5–10%	0.6 mg SC daily; increase weekly by 0.6 mg to 3.0 mg daily.	Nausea, vomiting, diarrhoea, injection-site reactions	MTC/MEN2, pregnancy
4	Phentermine/Topiramate ER	~8–10%	3.75/23 mg PO daily × 14 days, then 7.5/46 mg daily. Can titrate up to 15/92 mg daily.	Dry mouth, insomnia, paraesthesia, tachycardia, cognitive slowing	Pregnancy (teratogenic), glaucoma, hyperthyroidism
5	Naltrexone/Bupropion ER (Contrave)	~5–8%	Titrate over 4 weeks to 32 mg/360 mg daily (2 tablets twice daily).	Nausea, headache, insomnia, anxiety, hypertension	Seizure disorder, eating disorders, opioid use
6	Orlistat (Xenical)	~3–5%	120 mg PO three times daily with fat-containing meals.	Oily stools, faecal urgency, flatulence, fat-soluble vitamin deficiency	Chronic malabsorption, cholestasis
7	Phentermine	~3–8% (short-term data)	15–37.5 mg PO daily, usually morning.	Tachycardia, insomnia, anxiety, dry mouth	Cardiovascular disease, uncontrolled hypertension, hyperthyroidism, pregnancy

Practical Clinical Pearls

Highest Efficacy

Medication	Key Point
Tirzepatide	Current pharmacologic leader for weight loss. Many patients achieve bariatric surgery-level results (>20% weight loss).
Semaglutide	Strong evidence base, widely used, substantial cardiometabolic benefits.
Liraglutide	Less effective than semaglutide but useful when weekly injections are unavailable.

Most Useful in Specific Situations

Scenario	Preferred Medication
Type 2 diabetes + obesity	Tirzepatide or semaglutide
Cardiovascular risk reduction	Semaglutide (strongest current outcomes data in obesity)
Emotional eating / food cravings	Naltrexone-bupropion
Cost-sensitive option	Orlistat
Need rapid appetite suppression	Phentermine (short-term)
Binge-eating tendencies with obesity	Consider GLP-1 agonist; sometimes naltrexone-bupropion

Monitoring

Parameter	Frequency
Weight, BMI, waist circumference	Every 4–12 weeks
Blood pressure and pulse	Every visit (especially phentermine-containing regimens)
HbA1c and glucose	Every 3–6 months if diabetes/pre-diabetes
Renal function	Periodically with GLP-1 agents
Mood changes	With bupropion-containing regimens

Response Benchmarks

A useful pragmatic rule:

- **<5% weight loss after 3 months on therapeutic dose:** consider stopping or switching.
- **5–10% weight loss:** clinically meaningful improvement in metabolic risk.
- **>10% weight loss:** substantial improvements in diabetes, sleep apnoea, fatty liver disease, and blood pressure.
- **>15% weight loss:** often approaches outcomes previously achievable mainly with bariatric surgery.

Quick Memory Table

Drug	Approximate Weight Loss	Main Limitation
Tirzepatide	★★★★★	GI side effects, cost
Semaglutide	★★★★☆	GI side effects, cost
Liraglutide	★★★★☆	Daily injections
Phentermine/Topiramate	★★★★☆	Teratogenicity, CNS effects
Naltrexone/Bupropion	★★★☆☆	Nausea, seizure risk
Orlistat	★★★☆☆	GI intolerance
Phentermine	★★★☆☆	Limited long-term use, stimulant effects

Current Practical Hierarchy (2026)

1. Tirzepatide
2. Semaglutide
3. Phentermine/Topiramate ER
4. Liraglutide
5. Naltrexone/Bupropion ER
6. Orlistat
7. Phentermine (short-term use)

For most patients with obesity and no contraindications, tirzepatide or semaglutide are now considered first-line pharmacologic options because they provide the greatest and most durable weight loss along with broad metabolic benefits.