

Semaglutide

History and Background

Semaglutide is a GLP-1 (glucagon-like peptide-1) receptor agonist developed by Novo Nordisk. It was FDA-approved in 2017 for type 2 diabetes (brand name Ozempic) and in 2021 for chronic weight management (brand name Wegovy). Semaglutide represents a major advancement in obesity treatment, showing average weight loss of 15-20% in clinical trials. It works similarly to tirzepatide but activates only GLP-1 receptors (not GIP).

Primary Uses

Semaglutide is FDA-approved for chronic weight management in adults with obesity (BMI ≥ 30) or overweight (BMI ≥ 27) with weight-related conditions. Also approved for improving glycemic control in type 2 diabetes. Studied for cardiovascular benefits and potential neuroprotective effects.

How It Works

Semaglutide is a GLP-1 receptor agonist that mimics the natural GLP-1 hormone. It increases insulin secretion in a glucose-dependent manner, suppresses glucagon secretion, slows gastric emptying, and reduces appetite through central nervous system effects. The result is powerful appetite suppression, improved satiety, better glucose control, and significant weight loss.

Standard Protocol

Dosing: Start 0.25mg weekly for 4 weeks. Increase to 0.5mg for 4 weeks. Further increase by 0.5mg increments every 4 weeks. Maximum: 2.4mg weekly.

Administration: Subcutaneous injection once weekly. Inject in abdomen, thigh, or upper arm. Rotate injection sites.

Timing: Same day each week, any time of day. Consistency important.

Titration Schedule:

Weeks 1-4: 0.25 mg once weekly

Weeks 5-8: 0.5 mg once weekly

Weeks 9-12: 1.0 mg once weekly

Weeks 13-16: 1.7 mg once weekly (optional)

Maintenance: 2.4 mg once weekly (maximum dose)

Duration: Ongoing for weight management. Clinical trials up to 68 weeks. Long-term use common for maintaining weight loss.

What to Expect

Positive Effects (Week 1-2)

Appetite reduction begins within 24-48 hours for most. Significant hunger suppression by day 3-7. Reduced food cravings and "food noise." Portions naturally decrease. Energy often improves after initial adjustment period.

Timeline to Results

Appetite effects: 2-7 days. Initial weight loss: 2-4 weeks. Steady weight loss: 4-16 weeks. Significant results: 12-28 weeks. Average weight loss: 15-20% of body weight over 68 weeks at 2.4mg dose.

Dose Response

Higher doses generally produce more weight loss. Many achieve excellent results at 1.0-1.7mg. Optimal dose balances efficacy with tolerability. GI side effects increase with dose.

Pros

- FDA-approved with extensive clinical trial data
- Highly effective for weight loss (15-20% average)
- Once-weekly dosing convenient
- Improves glucose control and insulin sensitivity
- Reduces cardiovascular risk in some studies
- Dramatically reduces appetite and cravings
- Generally well-tolerated at proper titration
- Can preserve muscle better than diet alone
- May reduce food addiction behaviors

Cons

- Gastrointestinal side effects very common: nausea, vomiting, diarrhea, constipation
- Expensive without insurance coverage
- Requires weekly injections
- Needs refrigerated storage
- Potential rapid weight regain after stopping
- May cause fatigue or reduced energy initially
- Requires careful protein intake to preserve muscle
- Can cause dehydration if fluid intake inadequate
- Possible thyroid C-cell tumor risk (theoretical, seen in rodents)
- May worsen gastroparesis or severe GI conditions
- Supply shortages have been common
- Not suitable during pregnancy or breastfeeding

Who Should Consider It

Adults with obesity (BMI ≥ 30) or overweight with weight-related conditions. Those with type 2 diabetes needing weight loss. Individuals who have not achieved goals with lifestyle changes alone. People seeking FDA-approved, evidence-based treatment.

Who Should Avoid It

Personal or family history of medullary thyroid cancer or MEN 2 syndrome. History of pancreatitis. Pregnant or breastfeeding women. Severe gastroparesis or GI disease. Those with diabetic retinopathy (use caution). Individuals not committed to lifestyle changes.

Semaglutide should only be used under medical supervision. FDA-approved versions require prescription. Individual results vary. Not for research use as unapproved compound.

