

## Semaglutide — Basic Review Questions

1. What class of medication is semaglutide, and what is it used to treat?

Answer: Semaglutide is a GLP-1 receptor agonist (an incretin mimetic). It is FDA-approved for type 2 diabetes, chronic weight management/obesity, cardiovascular risk reduction, chronic kidney disease, and MASH (metabolic dysfunction-associated steatohepatitis). It is sold as Ozempic and Rybelsus for diabetes and as Wegovy for obesity, cardiovascular risk, and MASH.

2. How does semaglutide lower blood sugar, and why does it rarely cause hypoglycemia?

Answer: It increases insulin release and decreases glucagon, but only when blood glucose is elevated — a glucose-dependent effect. When glucose is normal or low, the drug stops driving insulin release, so it rarely causes low blood sugar on its own, unlike sulfonylureas or insulin. It also slows how quickly the stomach empties, which blunts the rise in glucose after meals.

3. How does semaglutide cause weight loss?

Answer: Mainly by acting on the brain's appetite centers in the hypothalamus, where it reduces hunger and increases the feeling of fullness. It also slows stomach emptying, so people stay full longer and tend to eat less. The appetite effect is the primary driver of weight loss.

4. Why can semaglutide be given just once a week, and how is the dose started?

Answer: It has a long half-life of about one week because it binds tightly to albumin in the blood, which slows its clearance. Treatment starts at a low dose (0.25 mg) and is increased slowly, advancing only when the current dose is well tolerated. Going slowly gives the body time to adjust and reduces nausea and other GI side effects.

5. What are the key clinical trial findings a clinician should know?

Answer: STEP showed roughly 15% weight loss in obesity. SELECT showed a 20% reduction in major cardiovascular events in non-diabetic patients with existing heart disease — the first weight-loss drug to prove a cardiovascular benefit. SUSTAIN-6 showed reduced cardiovascular events in type 2 diabetes. FLOW showed slowed progression of kidney disease. A Phase 2 NASH trial showed a high rate of liver-disease resolution. Together these support semaglutide as a cardiovascular, kidney, and liver agent — not just a diabetes or weight-loss drug.

6. What are the most common side effects, and what happens when a patient stops taking it?

Answer: The most common side effects are gastrointestinal — nausea, diarrhea, and vomiting — which are usually mild, occur mainly while the dose is being increased, and ease over time. Titrating slowly and staying well hydrated helps manage them. If the medication is stopped, most patients regain about two-thirds of the lost weight within a year, so it is generally used as a long-term treatment.