Cagrilintide — Basic Review Questions

1. What is cagrilintide, what class of medication is it, and what is its approval status?

Answer: Cagrilintide (also called AM833) is the first long-acting amylin analog — it works as a dual calcitonin/amylin receptor agonist and is given as a once-weekly subcutaneous injection. It is investigational and not yet FDA-approved. Its fixed-dose combination product, CagriSema (cagrilintide plus semaglutide), had an NDA filed in December 2025, with an FDA decision expected around October 2026. It is being developed mainly for obesity and type 2 diabetes.

2. How does cagrilintide work, and how is it different from a GLP-1 drug like semaglutide?

Answer: Amylin is a hormone released alongside insulin after meals that helps control appetite and post-meal glucose. It is deficient or dysregulated in diabetes and obesity, and GLP-1 drugs do not address it. Cagrilintide is a stable, long-acting version of amylin (native amylin cannot be made into a drug because it clumps together). Importantly, it acts on a different brain circuit than GLP-1 drugs — the hindbrain rather than the hypothalamus — so it adds a separate satiety signal instead of doing the same thing as semaglutide.

3. How does cagrilintide cause weight loss?

Answer: It acts on appetite centers in the hindbrain (the area postrema and connected nuclei) to increase the feeling of fullness and reduce how much a person eats. It also helps curb reward-driven, or "hedonic," eating — eating for pleasure or habit rather than hunger — which GLP-1 drugs address less directly. It slows stomach emptying as well. The overall effect is reduced appetite and food intake.

4. What is CagriSema, and why does combining cagrilintide with semaglutide work better than either drug alone?

Answer: CagriSema is a fixed-dose combination of cagrilintide and semaglutide given as a single weekly injection. It works better than either drug alone because the two act on different, complementary brain circuits — semaglutide on the hypothalamus (hunger-driven eating) and cagrilintide on the hindbrain and reward circuits (fullness and pleasure-driven eating). Because they engage separate pathways rather than the same receptor, the combined weight loss is greater than simply adding the two effects together (about 22.7% combined versus roughly 16% for semaglutide and 12% for cagrilintide alone in trials).

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

Answer: In the REDEFINE 1 obesity trial, CagriSema produced about 20–23% weight loss at 68 weeks — more than semaglutide (~15%) or cagrilintide (~12%) alone — and over 40% of patients lost at least 25% of their body weight. In type 2 diabetes trials (REDEFINE 2 and REIMAGINE 2), it produced large weight loss and strong HbA1c reductions, with most patients reaching target glucose levels. Notably, weight loss had not plateaued at 68 weeks. These results make CagriSema the most effective weight-loss regimen studied in a Phase 3 trial to date.

6. What are the most common side effects, and how is the dose managed?

Answer: The most common side effects are gastrointestinal — nausea, vomiting, diarrhea, and constipation — and they occur at higher rates than with GLP-1 drugs alone because the amylin pathway adds to the effect. They are mostly mild to moderate, happen mainly while the dose is being increased, and ease over time. The dose is started low and increased slowly over at least 16 weeks; going slower improves tolerability, and many patients do well at lower-than-maximum doses. Staying well hydrated and reducing any insulin or sulfonylurea doses helps lower the risk of side effects and low blood sugar.