MK-677 (Ibutamoren) — Basic Review Questions

1. What is MK-677, what type of compound is it, and what is its regulatory status?

Answer: MK-677 (also called ibutamoren) is a growth hormone secretagogue that activates the ghrelin receptor (GHS-R1a) — the same receptor target as ipamorelin. Importantly, it is technically not a peptide but a small, non-peptide molecule, which is what lets it be taken by mouth (it survives digestion, unlike the injectable peptides). It is not FDA-approved; development reached Phase II but never advanced to Phase III.

2. How does MK-677 work?

Answer: It binds the ghrelin receptor in the hypothalamus and pituitary and stimulates the body's own growth hormone (GH) release — increasing GHRH, reducing the somatostatin "brake," and directly prompting the pituitary to secrete GH. The GH then acts on the liver to raise IGF-1, which carries out GH's anabolic effects. So, like the injectable secretagogues, it amplifies the body's own GH production rather than supplying GH directly.

3. What is MK-677's defining advantage among GH secretagogues?

Answer: Its defining advantage is being the only oral growth hormone secretagogue that produces sustained GH elevation — a single daily oral dose keeps GH elevated for up to 24 hours, with no injection required. The injectable GHRPs (such as ipamorelin) have very short half-lives and cannot match that duration with daily dosing. MK-677 also has the deepest clinical-trial evidence base of the class, with multiple RCTs confirming reliable IGF-1 elevation.

4. How is MK-677 different from taking growth hormone directly?

Answer: Like the other secretagogues, it amplifies the body's natural pulses of GH and keeps the normal feedback system intact — high IGF-1 dampens further stimulation, so the effect is self-limiting. Injected synthetic GH, by contrast, bypasses the body's control entirely, creating continuous high levels that can downregulate GH receptors and antagonize insulin. MK-677 amplifies the physiology rather than replacing it.

5. What benefits are supported by trials, and what is the key dosing principle?

Answer: In clinical trials, MK-677 reliably raised IGF-1, increased lean (fat-free) body mass and reversed a catabolic (muscle-wasting) state, improved deep (slow-wave) sleep, and — combined with a bisphosphonate — added bone-building to the bone-preserving effect of the bisphosphonate. The key dosing principle is to use the lower 12.5 mg dose (not 25 mg) at bedtime: near-maximal GH effect occurs at about 10–12.5 mg, and the higher dose mainly adds side effects. Bedtime dosing aligns with the natural nighttime GH surge, and cycling (about 12 weeks on, then a break) helps avoid receptor desensitization.

6. What are the main risks and cautions, and what is the state of the evidence?

Answer: The main risks are metabolic and fluid-related. Because GH counteracts insulin, MK-677 can raise blood sugar and impair glucose tolerance, so glucose and insulin monitoring is essential, and pre-diabetic or diabetic patients should be stabilized

first (often with a GLP-1 drug). Fluid retention (edema) is the bigger issue: it is more pronounced than with short-acting injectables because of the sustained GH elevation, and concern about heart-failure/edema risk is actually why MK-677 never advanced to Phase III — so it is contraindicated in congestive heart failure. As with other GH-axis agents, active cancer is a contraindication. There is no Phase III or long-term safety data, so any use is investigational.