Melanotan I (Afamelanotide) — Basic Review Questions

1. What is Melanotan I, what type of peptide is it, and what is its regulatory status?

Answer: Melanotan I (generic name afamelanotide, brand Scenesse) is a synthetic peptide — a 13-amino-acid analogue of α-MSH (alpha-melanocyte-stimulating hormone), the body's natural pigment-stimulating hormone. It selectively activates the MC1R receptor on pigment cells. Unusually for this series, it has an approved form: it is FDA- and EMA-approved as an implant for a rare light-sensitivity disorder. Its widely known use for cosmetic tanning, however, is off-label and not approved anywhere.

2. How does Melanotan I work?

Answer: It binds the MC1R receptor on melanocytes (pigment cells) and turns on a cAMP signal that does more than tan the skin. That single signal branches into four arms: it drives production of eumelanin (the brown/black pigment that absorbs UV and visible light and mops up reactive oxygen), and — independently of pigment — it supports DNA repair, boosts antioxidant defenses (via Nrf2), and reduces inflammation (via NF-κB). In effect it switches on the skin's whole UV-defense program, not just darkening it.

3. What is Melanotan I approved for, and how strong is that evidence?

Answer: It is approved only for erythropoietic protoporphyria (EPP), a rare inherited disorder in which a light-reactive compound builds up and causes severe burning pain on sun exposure; by increasing protective pigment, Melanotan I lets these patients tolerate far more light. The evidence for this use is the strongest of any peptide in the skin group: multiple Phase 3 trials (showing more pain-free sun time and better quality of life), an 8-to-10-year safety record with no melanoma signal, and even a dose-dependent liver-protective effect. The approval is narrow, though — it covers only the 16 mg implant for adult EPP.

4. How does Melanotan I differ from Melanotan II?

Answer: They are different peptides and should not be confused (unregulated products often mislabel one as the other). Melanotan I is a 13-amino-acid peptide that is highly selective for the MC1R receptor, so it drives pigment and photoprotection essentially without sexual or appetite effects. Melanotan II is a smaller, cyclic peptide that non-selectively activates several melanocortin receptors (MC1R plus MC3/4/5R), giving a faster, more potent tan but also sexual arousal, appetite suppression, and nausea. In short, MT-I is the selective, approved, "clean" pigment/photoprotection peptide; MT-II is the broader, unapproved, more potent but more side-effect-laden one.

5. What is the concern with using Melanotan I for cosmetic tanning?

Answer: Cosmetic tanning is the way most people encounter "melanotan," but it is off-label and unvalidated — there are no randomized trials, no standardized dose (the empirical practice is roughly 250–500 mcg injected subcutaneously, but it is entirely anecdotal), and no long-term safety data in that population. The bigger real-world hazard is sourcing: unregulated melanotan products are not quality-controlled, are

frequently mislabeled (MT-I sold as MT-II and vice versa), and can be contaminated — enough that formal safety warnings have been issued.

6. What monitoring is required, and what is a key limitation to remember?

Answer: Because Melanotan I increases melanocyte activity and changes pigment and moles, twice-yearly full-body skin exams (with dermoscopy and documentation of moles) are mandatory, and a history of melanoma or premalignant/malignant skin lesions is a contraindication; it is also avoided in pregnancy, breastfeeding, and under age 18. Reassuringly, long-term monitored use has shown no melanoma signal — but that data comes from supervised patients, not unsupervised cosmetic users. A key limitation: the added pigment raises tolerance to light but does not make skin UV-proof, so sunscreen and sun protection are still required.