Thymosin Beta-4 (TB-4 / TB-500) — Basic Review Questions

1. What is Thymosin Beta-4 (TB-4 / TB-500), what type of peptide is it, and what is its regulatory status?

Answer: Thymosin Beta-4 (TB-4, sold synthetically as TB-500) is a 43-amino acid peptide the body makes naturally. Despite being grouped with the immune peptides, it is really a tissue-repair and regeneration peptide — its anti-inflammatory effects are a secondary feature. It is not FDA-approved (it holds only an orphan designation for a rare eye condition), is prohibited in sport by WADA at all times, and — importantly — was removed from pharmacy compounding (503A/503B) in 2023–2024, so it now sits outside the regulated compounding pathway.

2. How does TB-4 work?

Answer: Its central mechanism is regulating actin, one of the main structural proteins inside cells. TB-4 binds and "sequesters" free actin building blocks (G-actin), then releases them in a controlled way so cells can rebuild their internal scaffolding and migrate — the foundation of wound closure, new blood-vessel growth (angiogenesis), and tissue rebuilding. On top of this repair role, it calms inflammation by suppressing NF-κB (lowering TNF-α, IL-1β, IL-6, and others). The guide is careful to note that many other commonly claimed pathways (AMPK, mTOR, NAD/sirtuins, and so on) are not actually confirmed for TB-4.

3. How does TB-4 differ from the other immune-category peptides (TA1 and LL-37)?

Answer: It is the odd one out. TA1 modulates the adaptive immune system (T cells) and LL-37 is an antimicrobial peptide that shapes innate immunity — both are primarily immune agents. TB-4's defining job is physical tissue repair through actin dynamics, with immune-calming as a bonus rather than the main purpose. So while it shares the anti-inflammatory theme of the category, it is best framed for patients as a recovery/repair enhancer rather than an immune drug.

4. What is the best human evidence, and what remains unproven?

Answer: The cleanest human evidence is topical, not systemic. Eye-drop formulations reduced corneal damage and dry-eye symptoms with essentially no adverse events (and are near Phase III for a corneal nerve condition), and a topical gel sped up chronic wound healing by about a month in responders. The bigger systemic claims — cardiac regeneration, neuroprotection, anti-fibrosis — remain preclinical or, at best, positive only in a trial subgroup (a STEMI heart-attack study was significant in an early-treatment subgroup but not overall). So the confirmed wins are narrow and topical; the headline regenerative promises are not yet proven in humans.

5. Why is the lack of subcutaneous pharmacokinetic data so important?

Answer: Because subcutaneous (SC) injection is how TB-4/TB-500 is actually used in practice — yet every human clinical trial used either intravenous or topical routes. SC bioavailability, dosing, and kinetics have never been established in people, so the common SC regimens are anecdotal extrapolations from IV data, not evidence-based protocols. This is the single most important gap to disclose, and combined with its

removal from compounding it means sourcing and dosing both sit outside validated standards.

6. What are the main cautions and the safety profile?

Answer: Across more than 400 trial subjects, TB-4 was well tolerated — no dose-limiting toxicities or serious adverse events, only mild effects, zero adverse events in the eye-drop trials, and a very low (~1%) rate of transient anti-drug antibodies — but there is no long-term human safety data beyond about two weeks. The main theoretical caution stems from its pro-angiogenesis (blood-vessel-growing) activity: active cancer is treated as a theoretical contraindication, and it may work against anti-angiogenic (anti-VEGF) cancer therapies. Its active fragment (Ac-SDKP) is broken down by ACE, so ACE inhibitors may enhance its anti-fibrotic effect. Pregnancy and competitive (drug-tested) athletes are clear avoid situations.