TB-500 / Thymosin β4 Research Summary

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What the Research Suggests, in Plain Language

TB-500 is a short, lab-made piece of a natural protein called thymosin beta-4. Almost all of the research in people tested the full-length natural protein, not the TB-500 piece.

• In animal studies, results suggest thymosin beta-4 and related pieces may be linked to faster wound closure and better repair measures after injuries to the skin, heart, eye and nervous system.

• In people, small clinical trials of the full-length protein as eye drops reported mixed results. In one dry-eye trial, the main goals were not met, although some other measures improved. Other small trials of the full-length protein reported it was well tolerated.

• No published study has tested the TB-500 piece itself in people. Most human papers that mention TB-500 are about detecting it in anti-doping tests.

In short: the animal results and the full-length protein trials raise questions for further research. They do not show that TB-500 is safe or effective in people.

Overview

TB-500 is a synthetic fragment of thymosin beta-4 (Tβ4). Most human clinical data concern full-length Tβ4 candidates rather than the synthetic fragment.

What the Research Actually Presents

Full-length Tβ4 clinical candidates: Phase 2/3 and safety trials (RGN-259 eye drops and related candidates) have been published in dry eye, neurotrophic keratopathy (a nerve-related corneal condition), venous ulcers and healthy-volunteer safety studies. Results were mixed: in one phase 2 dry-eye trial (PMID 26056426), the primary endpoints were not met; some secondary endpoints improved.

Synthetic TB-500 fragment: Essentially no human efficacy data. Most human-context records are anti-doping or analytical; the fragment (Ac-LKKTETQ) appears mainly in doping-detection papers.

Animal studies (~117 records):

• Wound models: Researchers observed accelerated wound closure and improved tissue organization compared with controls.

• Cardiac injury models: Studies reported observations consistent with improved cardiac repair markers in the models tested.

• Corneal and neurologic models: Animals showed improved recovery or functional measures in those specific injury settings.

Approximately 46 “human” records measure endogenous Tβ4 levels (the body’s own Tβ4), not administration of the synthetic peptide.

What the Research Suggests

Clinical data exist for full-length Tβ4 candidates in the conditions tested, with mixed results on primary endpoints. These do not automatically apply to the synthetic TB-500 fragment.

In animal models, Tβ4-related peptides were associated with improved tissue-repair measures in wound, cardiac, corneal, and neurologic injury models. No completed human efficacy trials of the synthetic TB-500 fragment are identified.

Mechanism and Signaling Pathways (as described in the literature)

Preclinical literature describes Tβ4 and related fragments as binding actin (a structural protein inside cells), influencing cell migration, and participating in angiogenesis (new blood-vessel formation) and tissue repair processes in the models examined.

Research Landscape

Catalog: 332 records — 28 human randomized controlled trials (RCTs, including registry entries; mostly full-length Tβ4), 69 other human, 117 animal, 17 in-vitro, 79 reviews, 1 systematic review/meta-analysis, 21 other. 20 ClinicalTrials.gov entries.

Key Studies

• Sosne G et al. 2015 (Clinical Ophthalmology): phase 2 randomized trial, Tβ4 eye drops in dry eye; 72 subjects; primary endpoints not met, some secondary endpoints improved (PMID 26056426).

• Sosne G et al. 2015 (Cornea): small phase 2 randomized trial in severe dry eye (PMID 25826322).

• Sosne G et al. 2022: randomized, placebo-controlled trial in neurotrophic keratopathy (PMID 36613994).

• Ruff D et al. 2010: phase 1 safety study of full-length Tβ4 in healthy volunteers (PMID 20536472).

• Wang X et al. 2021: phase 1 study of recombinant human Tβ4 (NL005) in healthy volunteers in China; 54 subjects (PMID 34346165).

• Guarnera G et al. 2007: phase 2 randomized study design report, topical Tβ4 in venous ulcers (PMID 17495250).

• Registered RGN-259 trials: NCT02597803, NCT03937882, NCT05555589.

Safety Findings Reported in the Studies

Safety data primarily concern full-length Tβ4 candidates, which were reported as well tolerated in the small trials published. Long-term data specific to synthetic TB-500 are absent.

Limitations and Evidence Gaps

No human efficacy data for the synthetic TB-500 fragment. Most clinical evidence covers full-length Tβ4, mainly in eye and heart settings, with mixed primary endpoints.

Regulatory Status

Not an FDA- or EMA-approved drug (U.S. Food and Drug Administration; European Medicines Agency). Included in the Department of Health and Human Services (HHS) draft/interim 503A compounding enforcement-discretion policy (October 2026). Prohibited by the World Anti-Doping Agency (WADA).

References

Sosne G et al. 2015 (PMID 26056426); Sosne G et al. 2015 (PMID 25826322); Sosne G et al. 2022 (PMID 36613994); Ruff D et al. 2010 (PMID 20536472); Wang X et al. 2021 (PMID 34346165); Guarnera G et al. 2007 (PMID 17495250). Registered trials NCT02597803, NCT03937882, NCT05555589. Animal studies in the research catalog.

Evidence reviewed through November 2026 (PHX research catalog snapshot of PubMed, ClinicalTrials.gov and Europe PMC).

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