Thymulin (FTS-Zn)

A Clinical Learning Guide for Medical Providers

Serum Thymic Factor-Zinc • Zinc-Dependent Nonapeptide (9 aa) • Immune + Neuroendocrine

Evidence base at a glance: A zinc-dependent thymic nonapeptide with broad anti-inflammatory reach and a UNIQUE neuroendocrine profile. Two facts dominate everything else: (1) it is biologically INACTIVE without equimolar zinc, and (2) the human evidence base is essentially empty — ZERO human RCTs; all therapeutic data are animal/in vitro. NOT FDA-approved (research peptide). In US practice it is most commonly used topically for hair.

1. Peptide Profile

Name: Thymulin / Serum Thymic Factor-Zinc (FTS, FTS-Zn)
Classification: Zinc-dependent thymic metallopeptide (immunomodulatory + neuroendocrine)
Structure: Nonapeptide — 9 amino acids (Glu-Ala-Lys-Ser-Gln-Gly-Gly-Ser-Asn); ~857 Da peptide / ~921 Da zinc-bound
Zinc requirement: ESSENTIAL — equimolar Zn^{2+} (1:1); biologically inactive without it
Source: Thymic epithelial cells (TECs) exclusively; discovered by Bach & Dardenne, early 1970s, Paris
Half-life: ~10 minutes (free peptide); longer when nanoparticle-bound
Routes: Subcutaneous (clinical); research: intracerebroventricular, intratracheal; topical (hair) in US practice
FDA status: NOT approved — research peptide only; compounding-pharmacy sourced

A Critical Distinction: Thymulin vs Thymalin

Thymulin and Thymalin are different agents and are easily confused. Thymulin is a single, defined zinc-dependent NONAPEPTIDE (9 aa) from thymic epithelial cells, with a unique neuroendocrine role. Thymalin is a multi-peptide CALF-THYMUS EXTRACT (approved in Russia) used broadly for immune modulation/geroprotection. They share a thymic origin but differ in structure, mechanism, zinc dependency (only Thymulin requires zinc), and evidence base.

2. Modes of Action & Mechanisms

Thymulin is an immune modulator (not a blunt stimulant) that acts upstream of inflammatory transcription across several converging pathways, while uniquely also engaging the neuroendocrine system. Its activity is entirely contingent on zinc.

Zinc-Dependent Activation

- The inactive FTS nonapeptide binds Zn^{2+} in a 1:1 (equimolar) ratio to adopt its active 3D conformation (confirmed by NMR)
- Zinc deficiency = biological inactivity — this is not a modifier but an on/off switch
- In aging, metallothionein (MT I/II/III) overexpression sequesters zinc, reducing thymulin bioavailability — a proposed mechanism of thymic involution that zinc supplementation can partially reverse

Immune & Anti-Inflammatory Pathways

Pathway / Action	Effect
T-cell differentiation	Promotes intra- and extra-thymic T-cell maturation (CD4/CD8); enhances NK cytotoxicity; anti-apoptotic (↓ caspase-3, p-p53)
Cytokine regulation	↓ IL-1β, IL-6, TNF-α, IL-17, IFN-γ, IL-5; PRESERVES anti-inflammatory IL-10; ↓ TGF-β/VEGF/eotaxin in asthma

Pathway / Action	Effect
NF-κB	Stabilizes IκB-α (↓ phosphorylation), inhibits IKK complex, blocks p50/p52/RelA(p65) nuclear translocation
MAPK / PKC-θ	Inhibits p38, JNK, SAPK; reduces PKC-θ → dampens T-cell receptor signaling (modulation without full immunosuppression)

Unique Neuroendocrine Integration

- Acts as a hypophysiotropic peptide — interacts with the growth hormone, prolactin, ACTH, and gonadotropin axes
- Restores gonadotropins in thymulin-deficient mice; partially restores serotonin/melatonin disrupted by chronic inflammation

What makes thymulin distinctive: no other short peptide simultaneously modulates the GH, prolactin, ACTH, AND gonadotropin axes. This neuroendocrine-immune interface is its signature — and the basis for much of the research interest.

3. Points of Clinical Relevance

1. Zinc is a prerequisite, not an adjunct — correct it FIRST

Thymulin is completely inactive without equimolar zinc, so zinc status governs whether the peptide works at all. Practically: confirm and correct zinc (target serum >80 µg/dL) BEFORE initiating, co-dose 15–30 mg elemental zinc daily (bisglycinate or picolinate preferred), and recognize this takes 2–4 weeks. Skipping this step guarantees failure.

2. The evidence base is entirely preclinical — there are zero human RCTs

Every therapeutic claim — autoimmune, respiratory, neuroendocrine, anti-inflammatory — derives from animal or in vitro studies. There are no placebo-controlled human trials and no human pharmacokinetic data for thymulin as a standalone agent. This is the single most important framing point for any patient conversation.

3. Its neuroendocrine reach is genuinely unique among peptides

Thymulin's simultaneous modulation of the GH, prolactin, ACTH, and gonadotropin axes is unmatched by other short peptides. This makes it conceptually interesting at the neuroendocrine-immune interface (and underlies theoretical GH-secretagogue combinations), though the clinical translation remains unproven.

4. The ~10-minute half-life is a major practical limitation

Free thymulin is cleared in about 10 minutes, which constrains systemic utility and is why the most promising research uses nanoparticle (PBCA, CK30PEG) and gene-therapy delivery to extend exposure. Clinicians should be skeptical of sustained systemic effect from the free peptide alone.

5. Autoimmune use is the most interesting AND the most hazardous frontier

Animal models in type 1 diabetes (notably JNK normalization) and multiple sclerosis (EAE) are encouraging, but the human therapeutic window is unknown and active autoimmune flare is a contraindication given the theoretical risk of immune overactivation. Promising in theory; genuinely risky in practice.

6. Evening dosing is mechanistically grounded

Administration in the evening (≈6–8 PM) aligns with the circadian rhythm of thymic hormone secretion and supports stable trough levels — a small but mechanistically sensible protocol detail unique among these peptides.

7. In real-world US practice, the dominant use is topical for hair

Despite the systemic research interest, the most common actual US application is topical zinc-thymulin (~0.001% in creams/gels/drops, often with dermarolling) to support the hair follicle —

encouraging exit from telogen into anagen. This is worth knowing as the practical reality versus the speculative systemic uses.

4. General Dosing & Delivery Options

No FDA-approved dosing exists; all subcutaneous dosing is extrapolated from compounding protocols and animal data, with no human PK to support it. Zinc co-administration is mandatory. For educational context only.

Subcutaneous Protocol (extrapolated)

Stage	Dose	Timing	Notes
Starting	100 µg SC	Evening (6–8 PM)	First 1–2 weeks
Standard	250–300 µg SC	Evening	Maintenance
Advanced	up to 500 µg SC	Evening	Maximum; experienced protocols
Zinc co-dose	15–30 mg elemental	Daily, oral	ESSENTIAL — bisglycinate/picolinate

Topical (the common US use)

- Zinc-thymulin ~0.001% in creams, gels, or liquid drops, applied daily, often combined with dermarolling, to stimulate the hair follicle (telogen → anagen transition)

Research Delivery Platforms

- **PBCA nanoparticles:** extend the ~10-min half-life; more effective than free peptide in sepsis and EAE (mouse) models
- **CK30PEG DNA nanoparticles:** intratracheal thymulin gene delivery to airway epithelium — the platform already has human Phase I data in cystic fibrosis
- **Adenoviral vector (RAd-metFTS):** CNS/lung gene delivery with prolonged expression and a regulatable Tet-Off switch

Administration Notes

- Reconstitute with bacteriostatic water; refrigerate (2–8°C); use within ~5–7 days; do not freeze reconstituted peptide
- Likely to be a cycled peptide (e.g. ~3-month intervals); separate zinc from copper supplements by 2+ hours

5. Evidence Profile

Evidence tier distribution (14 references): 0 human clinical trials, 10 animal studies, 2 in vitro, 2 reviews. The base is preclinical only.

Anti-Inflammatory / Sepsis (animal)

- In chronic endotoxemia/sepsis models, thymulin (free or PBCA-nanoparticle) attenuated NF-κB translocation, reduced IL-1β/IL-6/TNF-α, preserved IL-10, and reduced caspase-3; nanoparticle > free peptide
- ICV thymulin suppressed NF-κB nuclear translocation in the hippocampus (validating a central anti-inflammatory effect)

Respiratory / Asthma (animal gene therapy)

- CK30PEG DNA-nanoparticle thymulin gene therapy prevented airway remodeling and, in a single dose, reversed key asthma pathology in mice — ↓ IL-13, eotaxin, TGF-β, VEGF, IL-5; ↑ IFN-γ; normalized lung compliance

Autoimmune (animal)

Model	Finding
EAE / multiple sclerosis	PBCA-nanoparticle thymulin reduced severity and protected against relapsing-remitting EAE; NF-κB inhibition + cytokine suppression
Type 1 diabetes (STZ)	Thymulin + peroxiredoxin-6 synergy reduced hyperglycemia, normalized cytokines, and (most strikingly) normalized JNK signaling

Neuroendocrine & Aging (animal)

- Thymulin gene therapy restored gonadotropins in deficient mice; partially restored serotonin/melatonin in chronic inflammation
- Thymulin declines with thymic involution; zinc supplementation restored activity and thymic cortex regrowth in aged mice

Critical gaps: ZERO placebo-controlled human trials; NO human pharmacokinetic data (all dosing extrapolated from animals); the autoimmune therapeutic window in humans is undefined; no chronic-administration, carcinogenicity, reproductive, or organ-toxicity data; biomarkers (CD4/CD8, zinc) are logical but not validated as thymulin-specific.

6. Clinical Considerations

Contraindications

- **Active autoimmune flare:** lupus, RA, MS, IBD — theoretical immune overactivation; avoid
- **Uncorrected severe zinc deficiency:** the peptide is inactive — correct first or it cannot work
- **Pregnancy & lactation:** no safety data — avoid
- **Active malignancy on checkpoint immunotherapy:** unknown interaction — avoid
- **Hypersensitivity / severe immunodeficiency / pediatric:** avoid (no data; mechanism-dependent)

Drug Interactions (all theoretical — no human data)

- Immunosuppressants (cyclosporine, steroids): theoretical antagonism / blunting of effect
- Immunostimulants: additive risk — monitor immune markers
- Zinc/copper supplements: coordinate zinc dosing; separate from copper by 2+ hours (competition); avoid chronic zinc >40 mg/day
- Checkpoint inhibitors: unknown — use extreme caution

Monitoring Parameters

Parameter	Target / Note	Rationale
Serum zinc	80–120 µg/dL	Essential for thymulin activity
RBC zinc	Intracellular status	More accurate than serum
Serum copper / ceruloplasmin	70–140 µg/dL	Zinc-copper competition
CD4, CD8, CD4:CD8	Improvement	Primary efficacy / immune balance
CRP, ESR, IL-6	Trending down	Inflammatory load / cytokine response
CBC with differential	Normal	Safety monitoring

Typical monitoring cadence: baseline, ~4–6 weeks (CD4/CD8, zinc, CRP recheck), and ~3 months (full panel including copper). Positive response = improved CD4:CD8 ratio + declining CRP/ESR + improved

zinc status + subjective improvement; discontinue at 3 months if no change, or sooner for autoimmune flare, hypersensitivity, zinc toxicity, or confirmed pregnancy.

Safety Profile

- No serious adverse events in animal models at high research doses; mild injection-site reactions and transient early fatigue reported anecdotally
- Watch zinc toxicity (metallic taste, nausea); long-term human safety entirely unknown

Regulatory Status

Thymulin is NOT FDA-approved and is a research peptide; any human use is investigational and requires explicit informed consent. Source quality matters given compounding-pharmacy sourcing.

7. Final Note

Thymulin is the most mechanistically intriguing yet least clinically proven peptide in this immune-regulation set. Its anti-inflammatory reach is broad (NF-κB, MAPK, JNK, PKC-θ), and its neuroendocrine integration — simultaneous modulation of the GH, prolactin, ACTH, and gonadotropin axes — is genuinely unique among short peptides. Its single most defining feature is also the simplest to act on clinically: it is biologically inert without equimolar zinc, so zinc correction is a non-negotiable first step.

The honest framing is that thymulin sits almost entirely in the preclinical realm. There are no human RCTs, no human pharmacokinetics, and a half-life so short that the free peptide's systemic utility is questionable without nanoparticle or gene-therapy delivery — which is where the most exciting work (asthma reversal, sepsis protection, autoimmune modulation in mice) actually lives. In current US practice, the dominant real-world use is topical for hair, not the speculative systemic indications. For the clinician, thymulin is best understood as a research-stage peptide with a unique mechanistic story and real promise in diabetes and lung disease — but one whose systemic clinical use today rests on extrapolation, demands zinc optimization and careful autoimmune screening, and should proceed only investigationally with full informed consent.

Bottom line: A unique zinc-dependent thymic nonapeptide bridging immune and neuroendocrine regulation, with broad anti-inflammatory mechanisms and promising animal data in diabetes, asthma, and autoimmunity — but ZERO human trials, no human PK, and a 10-minute half-life. Zinc correction is mandatory. Most real-world US use is topical (hair). Research/investigational only.

Selected References

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