

# M5.1 — Hormone-Optimization Peptide Reference Card

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## Hormone-Optimization Peptide Reference Card

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**Use:** Quick-reference card for clinicians who heard M5.1 mention that “peptide therapy can run alongside hormone optimization” and want to know which peptides are the hormone-optimization tools and how they fit alongside the weight-loss-peptide stack covered in M5.2–M5.7. **Companion to:** M5.1 (baseline-labs framing — “peptide therapy runs alongside hormone optimization, not after it”); M5.5 (Tesamorelin); M5.6 (CJC-1295 NO DAC + Ipamorelin).

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### The parallel-track model

The older “fix hormones first, then start peptides” sequencing is workable but is not the only valid model. The peptides on this card *are* peptides, and they are *also* hormone-optimization tools — GH-axis (Sermorelin, CJC-1295 + Ipamorelin, Tesamorelin), HPG-axis (Kisspeptin-10, Gonadorelin), and regenerative / immune (BPC-157, Thymosin alpha-1). A clinician addressing the weight-management axis (Module 5) and a co-existing hormonal-optimization axis (other modules, summarized here) in **parallel rather than sequentially** is a valid clinical pattern, particularly in the mixed-phenotype patient — who is most of them. This card is the bridge: it names which compounds the hormone-optimization armamentarium contains, what each one does, where the weight-loss-peptide stack and the hormone-optimization stack genuinely combine, and where the deep-dive lesson lives in the curriculum.

A note on what this card is *not*: it is not a substitute for the deep-dive lesson on any compound, and it is not a recipe for combining four or five peptides at once. The dosing ranges below are practitioner-consensus ranges drawn from the linked library profiles; clinical judgment about whether a given patient should be on any of these compounds — and which others they should be on alongside — is the clinician’s, made on the basis of the full lesson, the full lab panel, and the patient’s full clinical picture.

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### 1. Sermorelin

**Class:** GHRH(1-29) analog — short-acting **FDA status:** Previously FDA-approved as Geref Diagnostic; withdrawn 2008 for manufacturing reasons, not safety. Currently compounded only (503A).

**Mechanism (one paragraph):** Sermorelin is the synthetic N-terminal 29-residue fragment of native 44-amino-acid GHRH. It binds the GHRH receptor on anterior-pituitary somatotrophs (Gs/cAMP/PKA cascade), stimulating GH gene transcription and pulsatile GH release. Because somatostatin feedback remains intact, GH cannot rise to supraphysiological levels — the hypothalamic-pituitary feedback loop self-limits, which is the safety argument for GHRH analogs over exogenous recombinant GH. Half-life is short (~10–20 minutes), which is why bedtime dosing is preferred: the brief stimulation aligns with the natural nocturnal GHRH surge that drives sleep-associated GH release (PMID 18031173; PMID 18046908; PMID 8329825).

**Why it appears in weight-loss-peptide context:** Sermorelin sits in the same GH-axis category as CJC-1295 + Ipamorelin and Tesamorelin but is the lowest-amplitude, most-physiological, and longest-clinical-history option in that group. In the parallel-track model, a patient on a GLP-1 RA who has age-related GH-IGF-1 decline, sleep-architecture complaints, or anti-aging-driven goals — but who does not have the visceral-adiposity or lean-mass-loss problem that brings Tesamorelin or CJC/Ipamorelin into play — may have sermorelin on the hormone-optimization side of the chart independent of the weight-loss-peptide side. It is the GHRH analog clinicians reach for when the goal is gentle GH-axis restoration rather than visceral-fat targeting or anabolic counterforce.

**Typical clinical use:** - Indication / use case: anti-aging GH-axis restoration; sleep-architecture support; sarcopenia adjunct; pediatric GHD (historical, Geref era) - Dose range: 0.2–0.3 mg SubQ once daily at bedtime (adult anti-aging practice; from Geref labeling); 10 mcg/kg in the original 5-month aging RCT (PMID 9141536); oral capsule 500 mcg once daily at bedtime in the available oral formulation - Duration / cycling: continuous in many anti-aging practices; some practitioners use 5 days on / 2 days off or 3 months on / 1 month off to prevent tachyphylaxis - Monitoring: IGF-1 baseline and every 3 months; correct hypothyroidism first (blunts response); fasting glucose; thyroid panel

**Contraindications + cautions:** Active malignancy, acromegaly, pituitary tumors, diabetic retinopathy, pregnancy/nursing. Obesity itself blunts GH response to GHRH; elderly have naturally blunted response. Glucocorticoids reduce efficacy.

**Key references:** PMID 9141536 (Khorram, JCEM 1997 — 5-month aging RCT); PMID 18046908 (Walker, Clin Interv Aging 2006 — clinical review); PMID 18031173 (Kemp & Fielder, BioDrugs 2007 — systematic review of pediatric use); PMID 9360512 (Khorram, JCEM 1997 — immune effects in aging).

**Module placement:** No standalone deep-dive in Module 5. Sermorelin is referenced in M5.5 as a mechanism comparator to tesamorelin (different fragment length, no Hex modification, shorter half-life, older pediatric-GHD evidence base). A standalone deep-dive belongs in a future hormone-optimization module.

## 2. CJC-1295 (NO DAC) + Ipamorelin

**Class:** GHRH analog (extended via DPP-IV-resistant substitutions, no DAC — short half-life) + GHRP (selective GHS-R1a / ghrelin-receptor agonist), administered together **FDA status:** Neither compound is FDA-approved for any indication. Both are research-state compounds available through 503A compounding with FDA Category 2 listing (post-2023) imposing jurisdictional variation. CJC-1295 with DAC reached Phase 2 but development halted; ipamorelin reached Phase 2 for postoperative ileus (PMID 25331030) and did not advance.

**Mechanism (one paragraph):** CJC-1295 (NO DAC, also called Mod-GRF 1-29) is the 29-residue GHRH analog with four amino-acid substitutions conferring DPP-IV resistance and extending half-life from native GHRH's ~7 minutes to ~30 minutes. It engages the GHRH receptor on the somatotroph (cAMP/PKA — the "gas pedal," amplifying the release signal). Ipamorelin is a selective pentapeptide agonist of GHS-R1a — the same receptor ghrelin activates — engaging the phospholipase-C / calcium pathway and partially suppressing somatostatin (the "ignition key," initiating the secretory burst). Because the two compounds engage different receptors on the same cell, the combined administration produces a supra-additive GH pulse approximately 7–10× greater than either agent alone, with pulsatility preserved. Ipamorelin's defining clinical feature is selectivity: unlike GHRP-2, GHRP-6, or Hexarelin, it stimulates GH release without elevating cortisol, prolactin, or ACTH at therapeutic doses (PMID 9849822). Distinguish CJC-1295 NO DAC sharply from CJC-1295 with DAC, which is a different molecule with an albumin-binding MPA group, an ~8-day half-life, and a sustained-elevation rather than pulse-amplifying profile.

**Why it appears in weight-loss-peptide context:** This is the lean-mass-preservation compound stack for the GLP-1-driven-weight-loss patient. GLP-1 RAs and GIP/GLP-1 dual agonists drive total weight loss in which approximately 25–39% (depending on cohort, DEXA interpretation, and resistance-training adherence) is lean mass. CJC-1295 + Ipamorelin engages the GHRH-GH-IGF-1 axis to generate an anabolic signal (IGF-1 → PI3K/AKT/mTOR → skeletal-muscle protein synthesis) that runs as a counterforce to the catabolic pressure of caloric deficit. The evidence state for this specific use is mechanism-rationale-strong / clinical-trial-thin: no Phase 3 RCT specifically tests this combination as a semaglutide or tirzepatide adjunct for lean-mass preservation, and the lean-mass-preservation foundation in any GLP-1 protocol remains resistance training plus adequate protein intake. The peptide layer is an off-label adjunctive structure built on the mechanism logic plus practitioner observation.

**Typical clinical use:** - Indication / use case: lean-mass preservation during GLP-1-driven weight loss; body recomposition; sleep-associated GH-pulse amplification when dosed at bedtime; GH-axis support in age-related decline - Dose range: CJC-1295 NO DAC ~100 mcg + Ipamorelin ~100 mcg per injection, SubQ, in a fasted state (minimum 2 hours post-meal); 1–3× daily depending on protocol intensity. Pre-sleep dose is the highest-yield single injection (amplifies natural slow-wave-sleep GH pulse) - Duration / cycling: 8–12 weeks on / 4 weeks off is the typical cycling pattern; 5 days on / 2 days off micro-cycling is also used. The fasted-state administration is non-negotiable — food blunts the GH pulse - Monitoring: IGF-1 baseline and every 3 months (sustained elevation

above the age-appropriate reference range warrants dose reduction); fasting glucose / HbA1c (GH-axis activation can affect insulin sensitivity); thyroid panel

**Contraindications + cautions:** Active malignancy, acromegaly, active pituitary tumors. Caution in diabetics on insulin or oral hypoglycemics (monitor glucose); glucocorticoids may blunt GH response; somatostatin analogs will block GH release. Ipamorelin is the best-tolerated GHRP in class — no cortisol/prolactin concerns at therapeutic doses — which is why it is paired here rather than GHRP-2 or Hexarelin.

**Key references:** PMID 9849822 (Raun et al., 1998 — ipamorelin selectivity); PMID 16352683 (Teichman et al., JCEM 2006 — CJC-1295 human PK); PMID 17018654 (Ionescu & Bhatt, JCEM 2006 — pulsatile GH preservation); PMID 25331030 (Beck et al., 2014 — ipamorelin Phase 2 for postoperative ileus, the closest human RCT in the literature). Combination context is mechanism-rationale, not RCT-tested.

**Module placement:** M5.6 (“Lean Mass Preservation — CJC-1pamorelin + MOTS-c During GLP-1-Driven Weight Loss”) is the deep-dive. The compounds also appear in M5.10 case integration.

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### 3. Tesamorelin

**Class:** GHRH(1-44) analog — full-length GHRH with N-terminal trans-3-hexenoic acid (Hex) modification conferring DPP-IV resistance **FDA status:** FDA-approved (BLA022505). On-label indication: reduction of excess abdominal fat in HIV-infected adult patients with lipodystrophy. Marketed as Egrifta (2010, 1 mg/vial, discontinued); Egrifta SV (2019, 2 mg/vial, 1.4 mg daily dose); Egrifta WR (2024, 2 mg daily dose). The label contains an explicit Limitation of Use: “EGRIFTA SV is not indicated for weight loss management as it has a weight neutral effect.” Off-label use for visceral adiposity in non-HIV populations is off-label use of an FDA-approved drug — regulatorily distinct from research-use-only or 503A-compounded peptides.

**Mechanism (one paragraph):** Tesamorelin is the only FDA-approved GHRH analog. It binds the GHRH receptor on anterior-pituitary somatotrophs (Gas/cAMP/PKA → GH1 transcription and pulsatile release into the hypophyseal portal). Released GH engages hepatic GHR (JAK2/STAT5b → IGF-1 transcription). The terminal half-life is ~26–38 minutes — long enough to engage the GHRH receptor on a pulsatile-physiological timescale, short enough to preserve hypothalamic-pituitary feedback and avoid the supraphysiological IGF-1 signature of sustained exogenous GH. The mechanistically distinctive feature is **preferential visceral-adipose-tissue lipolysis**: the pulsatile-but-elevated GH profile mobilizes lipids from VAT preferentially over SAT, likely via differential β3-adrenergic receptor density, hormone-sensitive lipase activity, and perilipin-phosphorylation state in the two depots (PMID 22298602; PMID 31644039; PMID 41545261).

**Why it appears in weight-loss-peptide context:** Tesamorelin is the visceral-adiposity-targeting tool in Module 5. It is the second mechanism class — after the GLP-1 axis — that the clinician reaches for when the presenting concern is central abdominal fat with cardiometabolic comorbidity

(often with concurrent MASLD/MASH; often in the body-recomposition or post-induction-loss phenotype). In Falutz Phase 3 (PMID 18057338): VAT reduction –15.2% with tesamorelin vs +5.0% with placebo at 26 weeks, with no significant change in subcutaneous adipose tissue — confirming the visceral selectivity. In Stanley 2014 (PMID 25038357): significant reductions in hepatic fat fraction in HIV-associated NAFLD. The “weight neutral” label limitation is mechanistically accurate: tesamorelin redistributes adipose tissue rather than producing total-weight reduction, which means patient counseling that frames it as a “weight loss” drug is misaligned with both the mechanism and the label. The clinical claim it supports is **visceral-fat redistribution with cardiometabolic benefit at neutral total weight** — and that is the framing under which it pairs with a GLP-1 RA driving the total-weight loss.

**Typical clinical use:** - Indication / use case: on-label HIV-associated lipodystrophy; off-label visceral adiposity in non-HIV populations (with shared-decision-making about the off-label-population extrapolation); MASLD/NAFLD-associated hepatic fat - Dose range: Egrifta SV 1.4 mg SubQ once daily; Egrifta WR 2 mg SubQ once daily (FDA label); off-label functional-medicine practice 1–2 mg SubQ once daily before bedtime in a fasted state with 12–16-week cycles - Duration / cycling: FDA-approved use is continuous with periodic reassessment at 6 months; off-label cycling typically 12–16 weeks on / 8 weeks off - Monitoring: IGF-1 baseline and every 3 months; fasting glucose / HbA1c (glucose intolerance is a documented side effect — monitor in diabetics); rotate injection sites on the abdomen; ~50% of patients develop anti-tesamorelin antibodies (typically non-neutralizing — monitor IGF-1 response as the in-vivo readout of clinical activity)

**Contraindications + cautions:** Pregnancy (Category X — IGF-1 crosses placenta, absolute); active malignancy; pituitary tumor or cranial irradiation; hypopituitarism (requires pituitary reserve for response); known hypersensitivity. Common side effects: peripheral edema, arthralgia (~10–15%), myalgia, nausea, injection-site reactions. Reconstituted product must be administered immediately per FDA label — no multi-day stability.

**Key references:** PMID 18057338 (Falutz et al., NEJM 2007 — Phase 3 pivotal, 26-week); PMID 25038357 (Stanley et al., JAMA 2014 — visceral and liver fat RCT); PMID 22298602 (Falutz, drugs review 2012); PMID 41545261 (body composition meta-analysis, 2025).

**Module placement:** M5.5 (“Tesamorelin + AOD-9604 — Targeted Visceral & Adipose Fat Protocols”) is the deep-dive. Also appears in M5.10 case integration.

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## 4. Kisspeptin-10

**Class:** KISS1R agonist; HPG-axis modulator upstream of GnRH **FDA status:** Research only — not FDA-approved for any indication. WADA prohibited (S0 — non-approved substances).

**Mechanism (one paragraph):** Kisspeptin-10 (KP-10) is the C-terminal decapeptide of the parent kisspeptin-54 and the most potent bioactive fragment of the kisspeptin family. It agonizes KISS1R



(formerly GPR54) on GnRH neurons in the arcuate and anteroventral periventricular nuclei of the hypothalamus, triggering  $Gq/11 \rightarrow PLC-\beta \rightarrow IP3 \rightarrow$  intracellular calcium mobilization, which depolarizes the GnRH neuron and stimulates **pulsatile** GnRH release into the hypophyseal portal circulation. The pulsatility is the load-bearing pharmacological feature: pulsatile GnRH drives physiological LH and FSH release, which in turn drives gonadal steroidogenesis (testosterone in men, estradiol/progesterone in women) and gametogenesis. Synthetic GnRH agonists such as leuprolide cause receptor desensitization and paradoxical gonadal suppression with continuous administration; kisspeptin works one step upstream and preserves the pulsatile pattern that maintains reproductive function (PMID 34210598; PMID 36287566).

**Why it appears in weight-loss-peptide context:** Kisspeptin-10 is not a weight-loss peptide and does not pair directly with the GLP-1 stack on a mechanism level. It appears on this card because it is the upstream HPG-axis modulator in the hormone-optimization armamentarium — the tool for the patient whose hormone-optimization need is reproductive-endocrine restoration (hypothalamic amenorrhea, hypogonadotropic hypogonadism, low desire) rather than GH-axis or thyroid optimization. In the parallel-track model, a perimenopausal woman on a GLP-1 RA with concurrent low desire, or a male hypogonadotropic patient on a weight-loss-peptide protocol who wants HPG-axis support without exogenous testosterone, may have kisspeptin-10 on the hormone-optimization side of the chart entirely independent of the weight-loss-peptide side.

**Typical clinical use:** - Indication / use case: female hypoactive sexual desire disorder (HSDD); hypothalamic amenorrhea; male hypogonadism (LH/testosterone restoration without exogenous T); IVF trigger alternative to hCG with lower OHSS risk (research) - Dose range: 1–10 nmol/kg IV bolus or 0.1–1.0 nmol/kg/h IV infusion in published clinical trials (Dhillon group); 50–100 mcg SubQ off-label - Duration / cycling: single or short-term pulsatile administration for fertility triggers; intermittent dosing (2–3x per week) for sexual-health protocols off-label; practitioner cycling 4 weeks on / 2 weeks off; chronic daily administration has not been extensively studied - Monitoring: LH, FSH, total and free testosterone (men) or estradiol/progesterone (women) at baseline and at 4–6 weeks; symptom response

**Contraindications + cautions:** Hormone-sensitive malignancies (breast, prostate, endometrial — LH/testosterone/estrogen stimulation contraindicated); active pregnancy (theoretical hormonal-disruption risk; acute IVF-trigger use is under direct supervision and is the exception); PCOS (use with caution — may exacerbate hyperandrogenism). Pharmacological conflict with GnRH agonists/antagonists; may reduce efficacy of hormonal contraceptives. Pediatric use is diagnostic only (pubertal assessment).

**Key references:** PMID 34210598 (Abbara et al., Trends Mol Med 2021 — clinical potential review); PMID 36287566 (Comninou et al., J Clin Invest 2023 — HSDD in women); PMID 36735255 (Comninou et al., J Clin Invest 2023 — sexual brain processing in men); PMID 33196464 (Abbara et al., Lancet Diabetes Endocrinol 2020 — KP-54 as IVF trigger).

**Module placement:** No standalone deep-dive in Module 5. Deep-dive belongs in a future HPG-axis / sexual-health module.

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## 5. Gonadorelin

**Class:** Synthetic GnRH decapeptide; pituitary GnRH-receptor agonist **FDA status:** FDA-approved as Factrel (diagnostic GnRH stimulation testing); widely used off-label as a TRT adjunct to maintain testicular function and as an HCG alternative.

**Mechanism (one paragraph):** Gonadorelin is the synthetic form of the endogenous GnRH decapeptide (pGlu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-NH<sub>2</sub>). It activates the GnRH receptor on anterior-pituitary gonadotrophs, driving LH and FSH release. The pharmacology that matters clinically is the **pulsatility requirement:** continuous GnRH-receptor stimulation desensitizes the receptor and paradoxically suppresses the HPG axis (the mechanism by which leuprolide and goserelin produce chemical castration in prostate cancer). Pulsatile or intermittent administration (typically 2× weekly SubQ for the TRT-adjunct indication; every 90–120 minutes via pump for fertility induction) maintains gonadotropin stimulation, which in turn maintains Leydig-cell intratesticular testosterone production (preserving testicular size and function) and Sertoli-cell spermatogenesis support (preserving fertility) during exogenous TRT. The native half-life is very short (2–10 minutes), which is consistent with the pulsatile-physiological-signaling role of endogenous GnRH.

**Why it appears in weight-loss-peptide context:** Gonadorelin does not pair mechanistically with the GLP-1 stack. It appears on this card because a meaningful subset of male weight-loss-peptide patients are concurrently on TRT (the obesity / hypogonadism / metabolic-syndrome cluster), and gonadorelin is the peptide tool — alongside or as alternative to hCG — that the TRT clinician uses to preserve testicular function during exogenous-testosterone administration. In the parallel-track model, a male patient on tirzepatide + TRT may have gonadorelin on the hormone-optimization side of the chart specifically to prevent testicular atrophy and preserve fertility while the weight-loss-peptide side of the chart drives the body-composition change.

**Typical clinical use:** - Indication / use case: TRT adjunct (testicular maintenance during testosterone therapy); fertility preservation in men on TRT; post-cycle therapy support; female fertility (pulsatile pump induction); delayed puberty; GnRH stimulation testing (the on-label diagnostic use) - Dose range: 100 mcg SubQ 2× per week for the TRT-adjunct indication; 25–50 mcg SubQ or pulsatile IV pump (every 90–120 minutes) for female fertility induction - Duration / cycling: continuous while on TRT for the adjunct indication; the **pulsatile** dosing pattern is non-negotiable — daily dosing will suppress the axis - Monitoring: total and free testosterone, LH, FSH, estradiol; testicular exam; semen analysis if fertility preservation is the goal

**Contraindications + cautions:** Ovarian cysts / PCOS (FSH stimulation may worsen); hormone-sensitive tumors; hypersensitivity (rare). **Critical:** continuous (rather than pulsatile / intermittent) dosing paradoxically suppresses the axis — this is the pharmacological inversion-risk for the compound. Side effects: injection-site reaction, headache; nausea and abdominal discomfort at higher doses.

**Key references:** Primary-literature PMIDs are thin for the 2x weekly SubQ TRT-adjunct dosing pattern, which is practitioner-consensus rather than label-derived; the on-label diagnostic GnRH stimulation testing pattern (Factrel) is the labeled reference.

**Module placement:** No standalone deep-dive in Module 5. Deep-dive belongs in a future HPG-axis / TRT-coordination module.

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## 6. BPC-157

**Class:** Regenerative pentadecapeptide derived from a protective protein in human gastric juice; angiogenic / cytoprotective **FDA status:** Research-only; not FDA-approved. Listed as Category 2 bulk drug substance (excluded from 503A compounding under FDA's Bulks List rulemaking — verify current jurisdictional status). WADA prohibited (S0).

**Mechanism (one paragraph):** BPC-157 (Body Protection Compound-157) is a synthetic 15-amino-acid sequence (GEPPPGKPADDAGLV) derived from a protective protein found in human gastric juice. Its primary mechanism is upregulation of VEGFR2 and activation of the PI3K/Akt/eNOS cascade, promoting endothelial cell survival, nitric oxide production, and angiogenesis across GI mucosa, tendon, ligament, skeletal muscle, and cardiac tissue. A distinguishing feature is **homeostatic NO-system modulation:** BPC-157 normalizes NO levels contextually rather than unidirectionally, counteracting both hypertension and hypotension models via the Egr-1/NAB2 self-limiting feedback loop. Cytoprotective effects against NSAID-induced toxicity (intestinal-tight-junction stabilization, hepatoprotection, neuroprotection) and brain-gut axis activity (modulation of serotonergic and dopaminergic systems with peripheral administration producing central effects) round out the mechanism profile (PMID 30915550; PMID 34267654; PMID 34380875).

**Why it appears in weight-loss-peptide context:** BPC-157 is not a weight-loss or hormone-axis peptide. It appears on this card because the weight-loss-peptide clinician will routinely encounter the patient who is concurrently on a regenerative protocol — for tendon, GI, or musculoskeletal recovery — and needs the BPC-157 mechanism, dosing, and contraindication profile available at chart-side. The single highest-yield combined-context use case in Module 5 is the patient on a GLP-1 + CJC/Ipamorelin lean-mass protocol who is also progressing a resistance-training program (the lean-mass-preservation foundation) and develops tendon or joint symptoms in the loading progression. BPC-157 is the recovery-side tool for that patient — separate from but operationally co-located with the metabolic stack.

**Typical clinical use:** - Indication / use case: tendon/ligament repair; muscle-tear recovery; GI mucosal protection (especially NSAID-related); inflammatory bowel symptoms; wound healing; post-surgical recovery; preclinical neuroprotection (stroke, TBI — research-state only) - Dose range: 250–500 mcg SubQ or IM 1–2x daily (practitioner-consensus range extrapolated from animal studies); 250–500 mcg oral once daily (uses gastric-stability data); 10–20 mg IV single infusion in the n=2 safety pilot only (PMID 40131143); 10 mg intravesical in the n=12 interstitial cystitis pilot (PMID 39325560) - Duration / cycling: practitioner standard is 6 weeks on, 2 weeks off; no formal



cycling protocol exists in peer-reviewed literature – Monitoring: no specific lab monitoring established; functional recovery / symptom response is the primary endpoint

**Contraindications + cautions: Active malignancy is the load-bearing contraindication** — BPC-157 promotes angiogenesis via VEGFR2/Akt/eNOS, which is the same pathway that supports tumor vasculature. No direct cancer studies exist, but the mechanism concern is the basis for the contraindication. Patients with active cancer, history of cancer within 5 years, or cancer predisposition syndromes should not use BPC-157 without oncologist clearance. Theoretical interactions: may antagonize morphine analgesia; may reduce local-anesthetic potency; theoretical interaction with anticoagulants. Pregnancy/nursing: no safety data — not recommended.

**Methodological note:** >70% of published BPC-157 research originates from a single Croatian research group (Sikiric/Seiwerth, University of Zagreb); independent validation has begun (PMID 40005999, 2025) but the evidence base is preclinical-extensive / clinical-preliminary. The first proper Phase 2 RCT (NCT07437547, hamstring repair, n=120) is currently recruiting.

**Key references:** PMID 30915550 (Sikiric, wound healing review 2018); PMID 34267654 (Seiwerth, wound healing review 2021); PMID 40756949 (2025 orthopaedic sports-medicine systematic review — 36 studies, 35 preclinical / 1 clinical); PMID 40005999 (Józwia, 2025 — independent multifunctionality review).

**Module placement:** No standalone deep-dive in Module 5. BPC-157 belongs to a regenerative / recovery module. Operationally referenced in Module 5 only where the GLP-1 + CJC/Ipamorelin + resistance-training pattern produces musculoskeletal recovery demand.

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## 7. Thymosin alpha-1

**Class:** Endogenous 28-amino-acid thymic immunomodulatory peptide; dual-action Th1 stimulator and Treg inducer **FDA status:** Not FDA-approved in the USA. Approved in 35+ countries as ZADAXIN (thymalfasin) for chronic hepatitis B and adjuvant immunotherapy for several cancers. WADA prohibited (S0).

**Mechanism (one paragraph):** Thymosin alpha-1 (Tα1) is an endogenous N-acetylated 28-residue peptide naturally secreted by the thymus. Its therapeutic value lies in **dual immunomodulation:** it simultaneously stimulates Th1 responses against pathogens (upregulation of IL-2, IFN-γ, TNF-α; enhanced NK-cell cytotoxicity; enhanced CD8+ T-cell activity; dendritic-cell maturation; TLR9 agonism) and induces regulatory T-cells via the IDO / tryptophan-catabolism pathway, preventing the immune overactivation that pure Th1 stimulators would risk. The net effect is balanced immunity — pathogen clearance and anti-tumor activity without driving autoimmunity. Tα1 also supports thymopoiesis (thymic T-cell production), which is the basis for its anti-aging / immunosenescence positioning, since thymic involution is a load-bearing component of age-related adaptive-immune decline (PMID 27450734; PMID 36812669; PMID 41373628).

**Why it appears in weight-loss-peptide context:** Thymosin alpha-1 is not a weight-loss peptide, not a metabolic-axis peptide, and not a direct co-mechanism with GLP-1s. It appears on this card because immune optimization is a load-bearing parallel-track domain in the older / immunosenescent / chronic-infection / cancer-history patient who is concurrently on a metabolic protocol. The clinical positioning is straightforward: in the parallel-track model, a weight-loss-peptide patient with concurrent chronic HBV, immunosenescence-related infection susceptibility, or oncologist-cleared cancer-adjunct immune support may have Tα1 on the immune-optimization side of the chart entirely independent of the metabolic side. Honest qualification: the most rigorous recent evidence is mixed — the HBV and HCC adjuvant data remain positive (multiple meta-analyses; PSM HR 0.308 in HCC post-resection); the 2025 TESTS Phase 3 RCT in sepsis (n=1,089, BMJ) was **negative** for 28-day mortality, contradicting earlier positive meta-analyses (PMID 39814420). Cite the indication-specific evidence rather than a class-level “Tα1 works” framing.

**Typical clinical use:** - Indication / use case: chronic hepatitis B (on-label outside USA as ZADAXIN); immune support in immunosenescence and post-chemotherapy immune recovery; cancer adjuvant immunotherapy (HCC, melanoma, lung — oncologist-supervised); chronic-infection states; off-label anti-aging immune-restoration practice - Dose range: 1.6 mg SubQ 2x weekly (ZADAXIN label / chronic-condition standard); 1.6 mg SubQ 2x daily for 5–7 days in acute / critical care (the dosing schema used in the TESTS sepsis trial) - Duration / cycling: HBV protocol runs 6–12 months continuously per the ZADAXIN label; acute / critical care 5–7 days; no formal cycling required - Monitoring: CBC with differential, lymphocyte subsets if available, indication-specific markers (HBV-DNA, HBeAg for HBV; tumor markers for cancer adjuvant); symptom monitoring for the autoimmune-flare cautionary signal

**Contraindications + cautions: Organ transplant recipients (absolute)** — Th1 stimulation is contraindicated on immunosuppression and Treg induction may paradoxically enhance rejection risk. Autoimmune flares: use with caution — Th1 stimulation may worsen some conditions; flu-like symptoms for the first 1–2 weeks are an expected Th1-activation signal rather than a true adverse event. Drug interactions: immunosuppressants (mutual efficacy reduction); concurrent checkpoint-inhibitor immunotherapy (additive stimulation — under oncologist supervision). Pregnancy/nursing: insufficient data, not recommended. Excellent established safety profile from >20 years of ZADAXIN use across 35+ countries and >11,000 trial subjects (PMID 38308608).

**Key references:** PMID 27450734 (Tuthill, immune modulation review 2016); PMID 21272455 (IFN + Tα1 for HBV meta-analysis, 2011); PMID 33076834 (Entecavir + Tα1 for HBV cirrhosis meta-analysis, 2020); PMID 39814420 (TESTS Phase 3 RCT, sepsis, 2025 — negative primary endpoint, BMJ); PMID 36812669 (cancer therapy immunoregulation review, 2023).

**Module placement:** No standalone deep-dive in Module 5. Deep-dive belongs in a future immune-optimization module.

## Combination grid — where the hormone-optimization peptides genuinely combine with the Module 5 weight-loss stack

Hormone-optimization peptide	Highest-yield Module 5 combination context	Pattern
Sermorelin	GLP-1 patient with age-related GH decline / sleep complaints — sermorelin on the hormone-optimization side independently of the metabolic side	Parallel-track, mechanistically independent
CJC-1295 NO DAC + Ipamorelin	GLP-1 patient with documented lean-mass loss on DEXA or functional decline (grip / 5-STs) despite resistance training + protein	Adjunctive to GLP-1; M5.6 is the deep-dive
Tesamorelin	GLP-1 patient with predominant visceral-adiposity phenotype, MASLD/MASH, or post-induction visceral fat that did not respond proportionally to total weight loss	Adjunctive to GLP-1; M5.5 is the deep-dive
Kisspeptin-10	Perimenopausal female GLP-1 patient with low desire; male hypogonadotropic patient seeking HPG-axis support without exogenous T	Parallel-track, mechanistically independent
Gonadorelin	Male GLP-1 + TRT patient — gonadorelin preserves testicular function and fertility during exogenous-T administration	Parallel-track, mechanistically independent
BPC-157	GLP-1 + CJC/Ipamorelin + resistance-training patient who develops tendon or joint symptoms in the loading progression	Parallel-track, recovery-side
Thymosin alpha-1	Older or immunosenescent GLP-1 patient with chronic HBV, infection susceptibility, or	Parallel-track, mechanistically independent

Hormone-optimization peptide	Highest-yield Module 5 combination context	Pattern
	oncologist-cleared cancer-adjunct immune indication	

## Cross-cutting clinical pearls

1. **GH-axis stack overlap:** Sermorelin, CJC-1295 + Ipamorelin, and Tesamorelin all engage the GHRH-GH-IGF-1 axis. They are **not additive**; they are alternatives selected by phenotype (anti-aging / sleep → Sermorelin; lean-mass preservation during GLP-1 → CJC + Ipamorelin; visceral-fat targeting → Tesamorelin). Co-administration of two or more GH-axis compounds is rarely indicated and should be a deliberate clinical decision with IGF-1 monitoring.
2. **HPG-axis distinction:** Kisspeptin-10 acts on GnRH neurons (one step upstream); Gonadorelin acts on pituitary gonadotrophs (one step downstream). They engage the same axis at different levels and are typically alternatives rather than combinations. Kisspeptin preserves pulsatility through endogenous GnRH-neuron firing; gonadorelin preserves it through pulsatile-dosing discipline.
3. **The pulsatility theme:** Three of the seven compounds (Sermorelin, CJC-1295 NO DAC + Ipamorelin, Tesamorelin) explicitly preserve GH pulsatility; two (Kisspeptin-10, Gonadorelin) explicitly preserve LH/FSH pulsatility. Pulsatility is the load-bearing pharmacological feature that distinguishes these tools from exogenous hormone replacement and is the safety argument for using them rather than direct hormone administration in most settings.
4. **The cancer-mechanism contraindication thread:** Active malignancy is a contraindication for the GH-axis compounds (IGF-1 elevation), the HPG-axis compounds (hormone-sensitive tumor risk), and BPC-157 (angiogenesis). Thymosin alpha-1 is the **exception** — it has positive cancer-adjuvant evidence in HCC and is positioned as an oncologist-supervised adjunct rather than contraindicated. Do not generalize the cancer-contraindication framing across the card.
5. **Off-label / off-pathway discipline:** Of the seven, only Tesamorelin and Gonadorelin (as Factrel, for diagnostic use) are FDA-approved. The other five are 503A-compounded research-state compounds, and the regulatory landscape has been moving (post-2023 FDA Category 2 listings affecting CJC-1295 and Ipamorelin; ongoing Bulks-List rulemaking affecting BPC-157). Verify jurisdictional status before prescribing or dispensing.