ESSENTIALS OF PEPTIDE THERAPY IN AESTHETIC MEDICINE

CBAM Aesthetic Mastery Series



PRINCIPAL AUTHORS:

Dr. Reza Akef

Dr. Mohsen Talani

PRINCIPAL AUTHORS:

Dr. Reza Akef

Dr. Mohsen Talani MD, Anatomist

CO-AUTHORS:

Dr. Ramin Rezaei Nasab. MD

Dr. Mehrsa Askari. MD

ABOUT AUTHORS



Dr. Reza Akef is a highly experienced and respected cosmetic physician, with over 15 years of experience in teaching and practicing cosmetic medicine. He is currently the Assistant Professor at McMaster University and the Chairman of the Canadian Board of Aesthetic Medicine (CBAM), where he shares his knowledge and expertise with other healthcare professionals to provide the best care for their patients.

Dr. Akef is board certified by the College of Family Physicians of Canada in both Family and Emergency Medicine. Additionally, he is deeply involved in interventional pain practice cooperation for the treatment of Migraines, chronic pain, TMJ, Myofascial pain, and Fibromyalgia. He is a leading cosmetic physician and an internationally recognized specialist in non-surgical cosmetic procedures.

Dr. Akef is dedicated to understanding his clients' concerns and creating personalized treatment plans that meet their needs and goals. He is committed to thoughtfully and strategically creating individualized combinations of leading, safe treatments that exceed client expectations. He is also the founder of Angel Gloss spa in Toronto, an established, leading destination for non-surgical cosmetic procedures for individuals seeking leading physicians with proven experience, the latest technology, and cutting-edge techniques.

Dr. Akef is actively involved in multiple training courses, webinars, and conferences all around the world, including prestigious international conferences such as IMCAS, AMWC, and Dubai Derma. He participates as a speaker at these events and is always looking to stay up to date with the latest developments in the field of cosmetic medicine.

Mohsen Talani is the Director of CBAM. He has over 18 years of experience teaching anatomy in Canada and internationally to students and healthcare practitioners in different fields of medicine such as physicians, dentists, nurses, chiropractors, and physiotherapists.

After graduating from medical school at a young age, he became a medical doctor in his home country, Iran, and practiced in the field of emergency medicine. While pursuing his Master's thesis in neuroscience at McGill University, he discovered his passion for teaching. Since then, he has been working in the field of medical science education, with a focus on anatomy.

He strongly believes that with the rapidly growing aesthetic industry, all practitioners should have a profound knowledge of skin basics, fat compartments, muscles, blood vessels, and nerves, in order to provide safe and effective care to clients and prevent or minimize post-treatment complications linked to lack of anatomy knowledge.

He is currently training healthcare practitioners who seek to have a deep knowledge of anatomy. He incorporates fun, innovative, and easy-to-understand methods of teaching in all of his classes, guest lectures, and presentations. Additionally, he supervises the cadaver lab dissections and hands-on practicals.



TABLE OF CONTENTS

FRONT MATTER 6

PART I. FOUNDATIONS 12

Chapter 1. Peptides 101: Structure, Classification, and How They Work 13

Chapter 2. Pharmacokinetics: Absorption, Half-Life, and Routes of Delivery 21

Chapter 3. Reading the Evidence: Triaging Any Peptide from Proven to Hype 31

Chapter 4. The Regulatory Landscape: FDA Status, 503A vs. 503B, Category 2, and the Gray Market 35

Chapter 5. Sourcing, Reconstitution, Dosing Math, and Injection Technique 41

PART II. THE PEPTIDES 46

Chapter 6. Skin and Anti-Aging Peptides 48

Chapter 7. Hair Restoration Peptides 54

Chapter 8.Recovery and Wound-Healing Peptides 61

Chapter 9. Weight Loss and Metabolic Peptides 67

Chapter 10. Growth Hormone Axis Peptides 74

Chapter 11. Sexual Health, Cognition, and Longevity Peptides 82

CBAM PUBLICATIONS
Canadian Board of Aesthetic Medicine

TABLE OF CONTENTS

PART III. CLINICAL PRACTISE 89

Chapter 12. Patient Selection, Consultation, and Informed Consent 90

Chapter 13. Titration, Monitoring, and Managing Adverse Events 95

Chapter 14.The Aesthetic Crossover and Combination Protocols 101

Chapter 15. Hair Loss: Classification and Pathophysiology 105

BACK MATTER 110

Master Dosing Tables 110

Peptide Status-at-a-Glance Chart 113

Anti-Doping Quick Reference (WADA) 115

Glossary 117

How to Verify Current FDA and WADA Status 120

Key References 121

CBAM PUBLICATIONS
Canadian Board of Aesthetic Medicine



Preface

Peptide therapy has arrived in aesthetic medicine faster than the evidence, the regulations, or the training has been able to keep pace. Patients walk into clinics asking for compounds by name — sometimes compounds their practitioner has never heard of — armed with claims from forums, influencers, and sellers whose interest is the sale, not the outcome. The result is a field moving at the speed of marketing while the science, in many cases, is still catching up.

This handbook exists to close that gap. It is written for the licensed practitioner who wants to offer peptide therapy well — to know which peptides are backed by real human evidence and which rest on animal data and hope, which are FDA-approved and which are legally precarious, what to actually prescribe and monitor, and when the right answer is simply "no." It is not a catalog of everything on the market, and it is not a sales tool. It is a working reference for clinical judgment.

Two commitments run through every page. The first is honesty about evidence: this book distinguishes proven clinical outcomes from biomarker changes and marketing narratives, and it says plainly when the data is thin. The second is regulatory and legal defensibility: it treats compliance not as a bureaucratic afterthought but as a core clinical competency. A practitioner who internalizes both will be able to navigate this field with confidence long after any single peptide's status has changed.

The goal is not to make you enthusiastic about peptides. It is to make you good at using them.



How to Use This Book

This is a reference, not a narrative. It is built to be opened to the page you need, not read cover to cover — though the foundations in Part I will make everything that follows more useful.

Part I — Foundations establishes the thinking: what peptides are, how they behave in the body, how to triage any peptide's evidence, the regulatory framework that governs what you can legally prescribe, and the practical mechanics of sourcing, reconstitution, dosing math, and injection. Read this part first. It contains the skills that let you evaluate peptides this book doesn't even cover.

Part II — The Peptides is the core. Each peptide is presented in a fixed format so you can find what you need fast and compare across compounds:

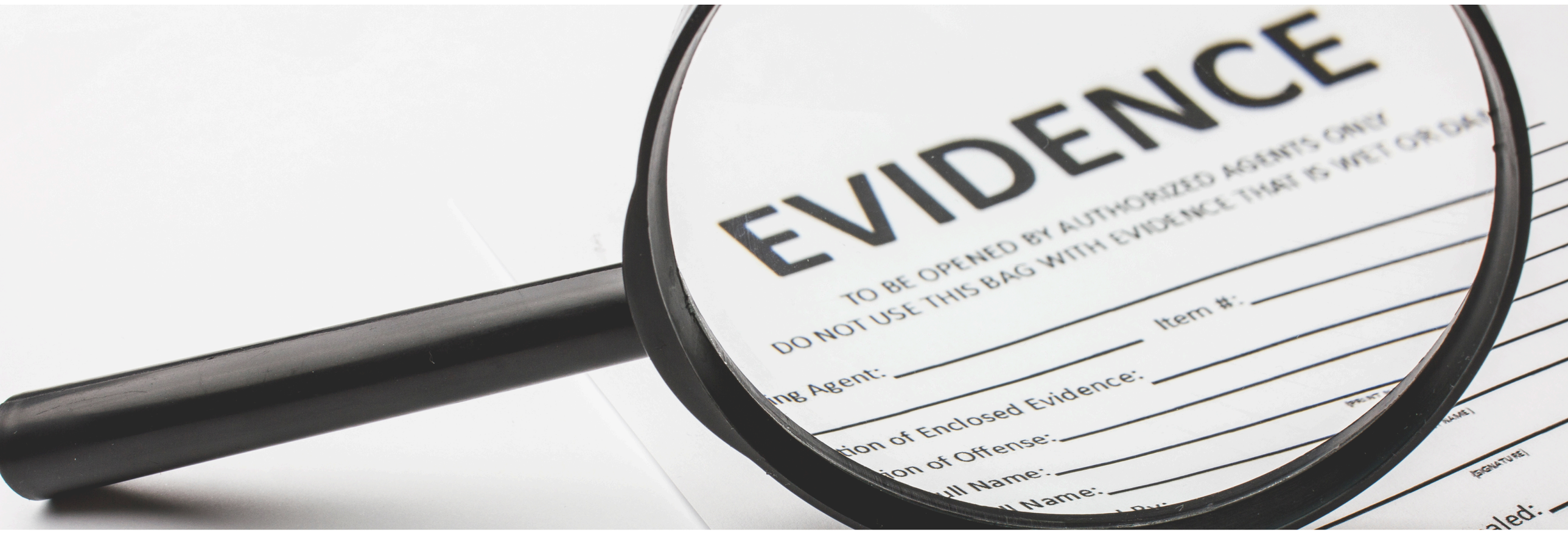
- **Status box** — FDA approval, regulatory category, and anti-doping status, up front
- **Mechanism** — how it works, briefly
- **Evidence** — what the human data actually shows
- **Dosing** — approved regimens where they exist; clearly labeled reference ranges where they do not
- **Monitoring** — what to track
- **Cautions** — contraindications and red flags
- **Counseling** — what to tell the patient

Part III — Clinical Practice covers the work around the prescription: patient selection and consent, titration and monitoring, the aesthetic crossover, and how to build a compliant practice.

Back Matter holds the quick-reference tools — master dosing tables, a status-at-a-glance chart, an anti-doping reference, a glossary,

and instructions for verifying current regulatory status.

A note on the dosing information: where a peptide is FDA-approved, this book gives the approved regimen. Where a peptide is not approved but a dose is commonly cited in the literature or compounding practice, that dose is included and explicitly labeled as a non-approved reference — so you can recognize what patients are encountering and make an informed decision, not so that you treat it as an endorsement.



A Note on Evidence and Regulation

Two truths shape how this book should be read.

Evidence is a spectrum, not a verdict. A compound can have an elegant mechanism, promising animal studies, and enthusiastic users — and still lack the human trial data that would make it genuinely proven. Throughout this handbook, you will see peptides placed along a range from *proven* (strong human trials and FDA approval) through *plausible* (real mechanism, limited human outcomes) to *hype* (marketing claims with preclinical or no data). A mechanism that "makes sense" is a hypothesis, not a result. The most valuable skill this book can give you is the habit of asking, for any peptide, *what is the human evidence, and how good is it?*

Regulatory status is a snapshot, not a fact. The legal standing of a peptide can change quickly — driven not by new science but by new regulatory determinations, shortage listings, and enforcement decisions. A compound that is legally compoundable in one quarter can be precarious the next. Every status statement in this book reflects a particular moment, and several of the peptides discussed are actively under review. Because of this, the book repeatedly directs you to verify current status before prescribing, and the back matter explains how. Treat any specific status claim here as a starting point for your own verification, not a substitute for it.

These two principles — evidence honesty and regulatory humility — are what separate a defensible peptide practice from a reckless one.



Safety and Legal Disclaimer

This book is an educational reference for licensed healthcare practitioners. It is not medical advice, and it does not establish a standard of care. Nothing in it should be used to diagnose or treat any individual patient without the independent clinical judgment of a qualified, licensed practitioner who has evaluated that specific patient.

The information here — including mechanisms, evidence summaries, dosing ranges, and regulatory statements — is provided for general educational purposes and may become outdated. Drug approvals, compounding rules, regulatory categories, and anti-doping classifications change frequently. Before prescribing, compounding, administering, or recommending any peptide, the practitioner is responsible for verifying the current FDA approval status, applicable compounding regulations, product labeling, and, where relevant, anti-doping rules, and for complying with all federal, state, and local laws and the requirements of their professional licensing body.

Dosing information for non-FDA-approved peptides is presented solely to inform practitioners of ranges cited in the literature and in compounding practice. Its inclusion is not an endorsement, a recommendation, or a representation that such use is safe, effective, or legal. Many of the peptides discussed in this book are not approved for human use, are designated by the FDA as substances that should not be compounded, and/or are prohibited in athletic competition.

The author and publisher make no warranties regarding the accuracy, completeness, or currency of this material and disclaim any

liability arising from its use. The practitioner assumes full responsibility for all clinical and prescribing decisions. By using this handbook, you acknowledge that peptide therapy carries inherent and in some cases unknown risks, and that the responsibility for safe, legal, and ethical practice rests entirely with you.

Part I

Foundations

1



PEPTIDES 101: STRUCTURE, CLASSIFICATION, AND HOW THEY WORK

What a Peptide Is

A peptide is a short chain of amino acids linked by peptide bonds — chemically the same building blocks as proteins, just smaller. The convention is loose but useful: chains of roughly 2 to 50 amino acids are called peptides; longer chains fold into the complex three-dimensional structures we call proteins. Insulin, at 51 amino acids, sits right at that boundary and is often described either way.

This size matters clinically. Peptides are large enough to carry specific biological instructions — they fit receptors with precision, like a key cut for one lock — but small enough to be synthesized, modified, and manufactured at scale. That combination of specificity and manufacturability is exactly why the category has exploded.

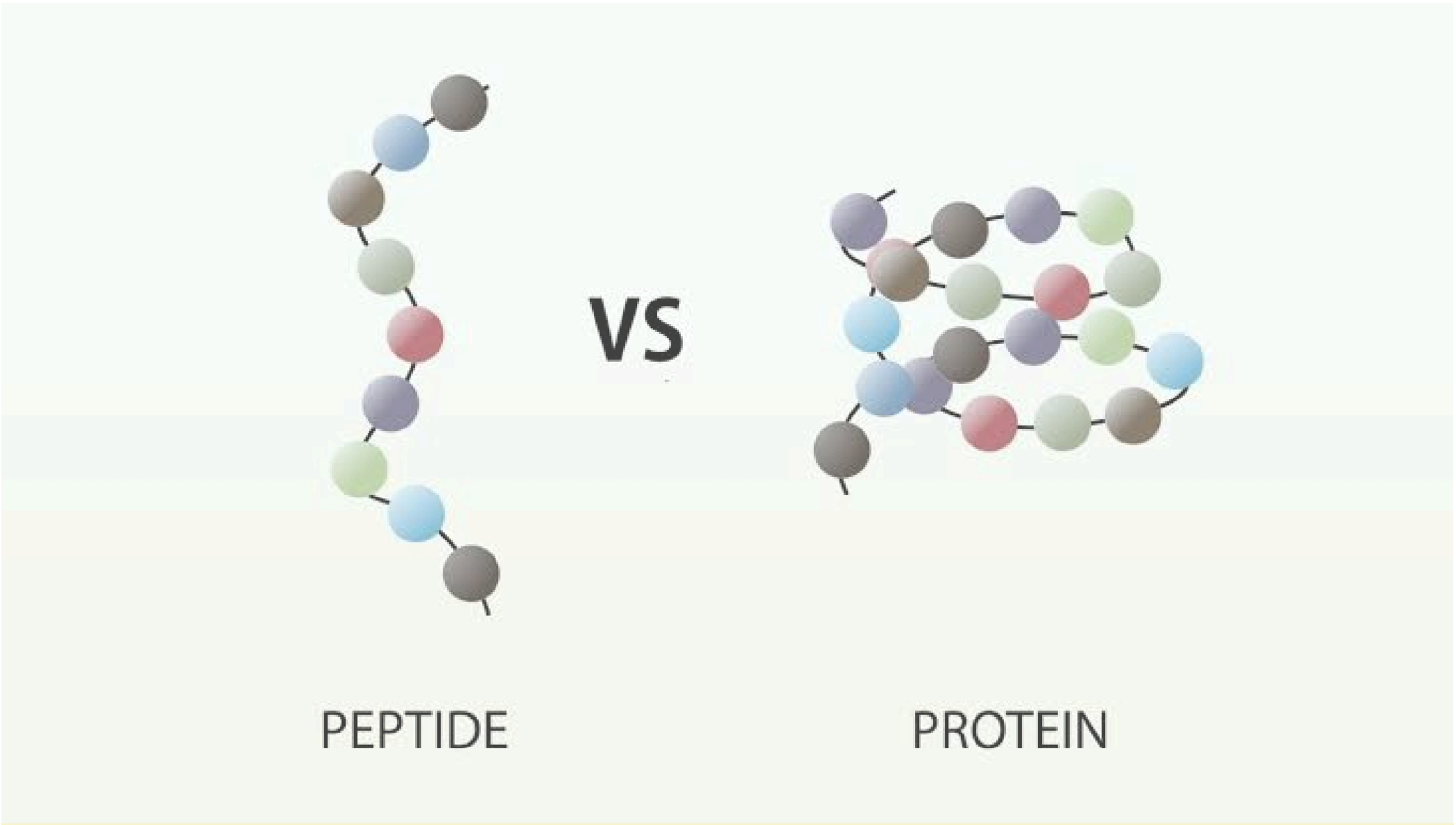


Figure 1.1 — A peptide is a short chain of amino acids linked by peptide bonds; longer chains fold into proteins. This size difference underlies both their specificity and their manufacturability."

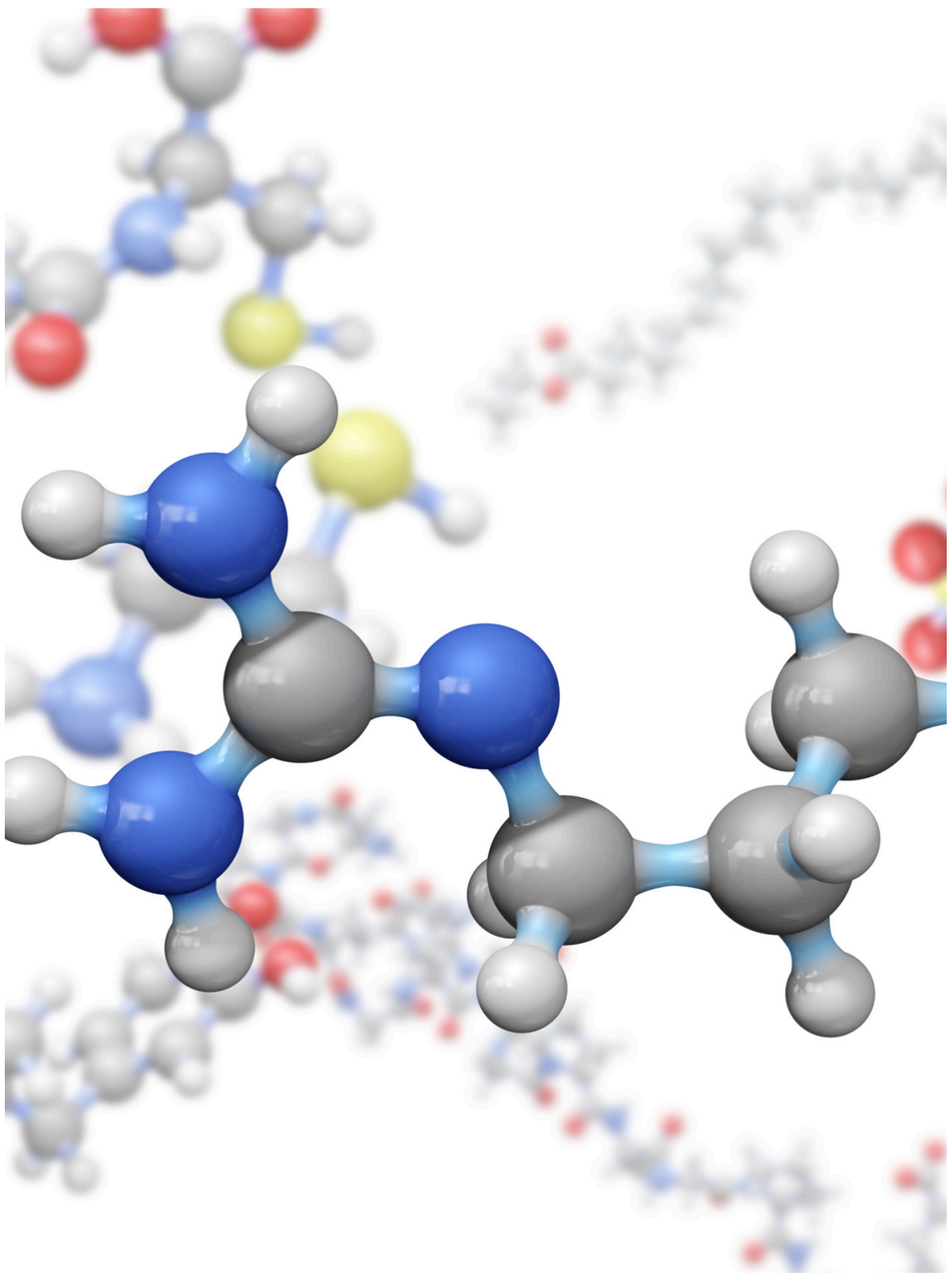
The body runs on peptides. Hormones (insulin, glucagon, growth hormone–releasing hormone), signaling molecules, and regulatory factors are peptides or proteins. Therapeutic peptides work by mimicking, blocking, or amplifying these natural signals. Understanding a peptide therefore starts with a single question: what natural signal is this molecule imitating or interrupting? Answer that, and its effects — and its side effects — usually follow logically.

How Peptides Are Built and Named

Each amino acid in the chain has a sequence position, and that sequence determines the peptide's shape and function. Change one amino acid and you can change everything — potency, half-life, receptor selectivity, or whether the molecule works at all.

This is why so many therapeutic peptides are *analogs* — deliberately modified versions of natural peptides. A natural hormone might be broken down in minutes; a single amino acid substitution or an added chemical group can extend that to days. Semaglutide, for example, is a GLP-1 analog engineered with a fatty-acid chain that binds albumin in the blood, stretching its half-life to about a week and enabling once-weekly dosing. The natural hormone it mimics lasts only minutes. The modification is the therapy.

Naming in this field is inconsistent and worth a caution. Peptides may go by a research code (AOD-9604, CJC-1295, TB-500), a generic drug name (semaglutide, tesamorelin, bremelanotide), or a brand name (Wegovy, Egrifta, Vyleesi). One compound can carry all three. Recognizing that "TB-500," "thymosin β-4 fragment," and various brand labels may point to related — or not quite identical — molecules is part of reading this field accurately.



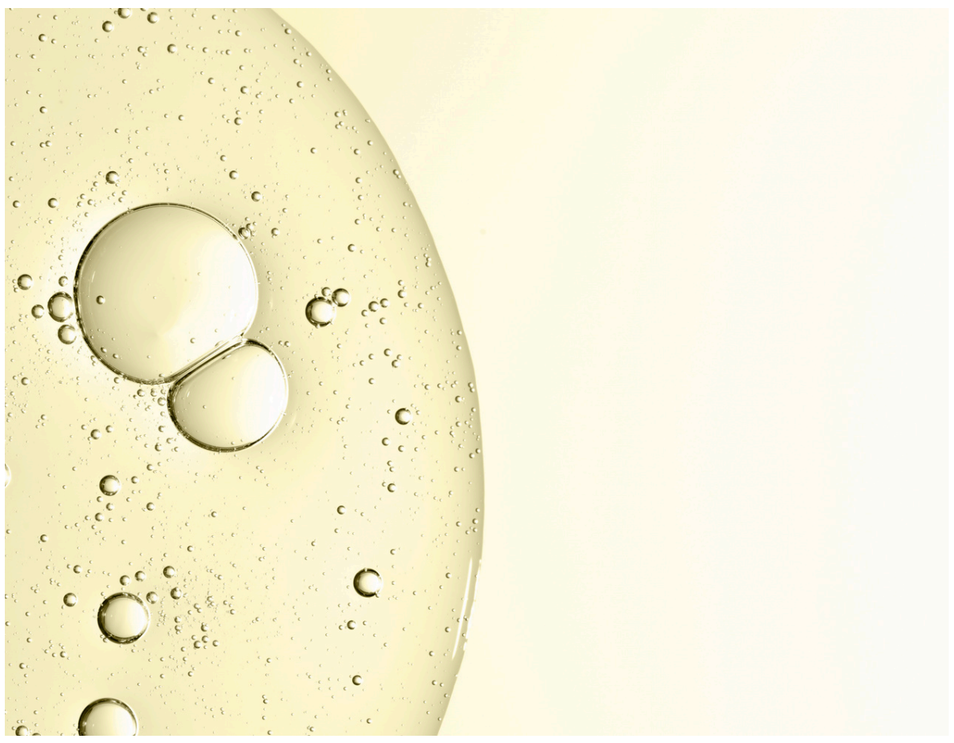
A small but important literacy point: not everything sold as a "peptide" is one. Some popular compounds in this space, such as MK-677 (ibutamoren) and 5-Amino-1MQ, are small molecules, not peptides at all. When a catalog labels a small molecule a "peptide," that is usually a sign of marketing-driven framing rather than scientific accuracy.

Classifying Peptides

There is no single official taxonomy, but for clinical purposes peptides are most usefully grouped by what they do — their functional target. This is the organizing logic of Part II of this book. The major functional classes a practitioner will encounter are:

- **Skin and structural peptides** — signal collagen production or modulate the neuromuscular junction (e.g., GHK-Cu, Matrixyl, Argireline)
- **Regenerative and wound-healing peptides** — promote tissue repair and angiogenesis (e.g., BPC-157, TB-500/thymosin β-4)
- **Metabolic peptides** — act on incretin and appetite pathways for weight and glucose control (e.g., semaglutide, tirzepatide)
- **Growth hormone axis peptides** — stimulate the body's own growth hormone release (e.g., sermorelin, CJC-1295, ipamorelin, tesamorelin)
- **Sexual health, cognitive, and longevity peptides** — act centrally on desire, mood, cognition, or immune and aging pathways (e.g., PT-141, semax, selank, thymosin α-1, epitalon)

A second, cross-cutting distinction matters for daily practice: route of administration. Peptides may be delivered subcutaneously (the most common), intramuscularly, intranasally, orally, or topically. Most peptides are poorly absorbed orally because the digestive tract breaks them down — which is why injection dominates the field, and why oral or topical formulations always raise the question of whether enough drug actually reaches its target. (Pharmacokinetics is the subject of Chapter 2.)



Class	What They Do	Representative Peptides	Covered In
Skin & structural	Signal collagen synthesis or modulate the neuromuscular junction	GHK-Cu, Matrixyl, Argireline	Ch. 6
Regenerative & wound-healing	Promote tissue repair and angiogenesis	BPC-157, TB-500/thymosin β-4	Ch. 8
Metabolic	Act on incretin and appetite pathways	Semaglutide, tirzepatide	Ch. 9
Growth hormone axis	Stimulate the body's own GH release	Sermorelin, CJC-1295, ipamorelin, tesamorelin	Ch. 10
Sexual health, cognition & longevity	Act centrally on desire, mood, cognition, immunity, aging	PT-141, semax, selank, thymosin α-1, epitalon	Ch. 11

Table 1.1 — Functional Classes of Peptides

A third distinction is regulatory, and it cuts across every functional class: whether a peptide is FDA-approved, compounded under a recognized pathway, or sold on the gray market. Two peptides with similar biology can occupy completely different legal worlds. This distinction is so central. that Chapter 4 is devoted to it — but it is worth flagging now that functional class tells you what a peptide does, while regulatory status tells you whether you can legally use it. Both questions must always be asked.

How Peptides Work: The Receptor Principle

Almost every therapeutic peptide works the same fundamental way: it binds a receptor and triggers a downstream effect.

Receptors are proteins, usually on the cell surface, shaped to recognize specific signaling molecules. When a peptide binds its receptor, it initiates a cascade inside the cell — switching genes on or off, releasing hormones, contracting or relaxing tissue, or altering metabolism. The peptide itself rarely does the work directly; it delivers a *message* that the cell then acts on.

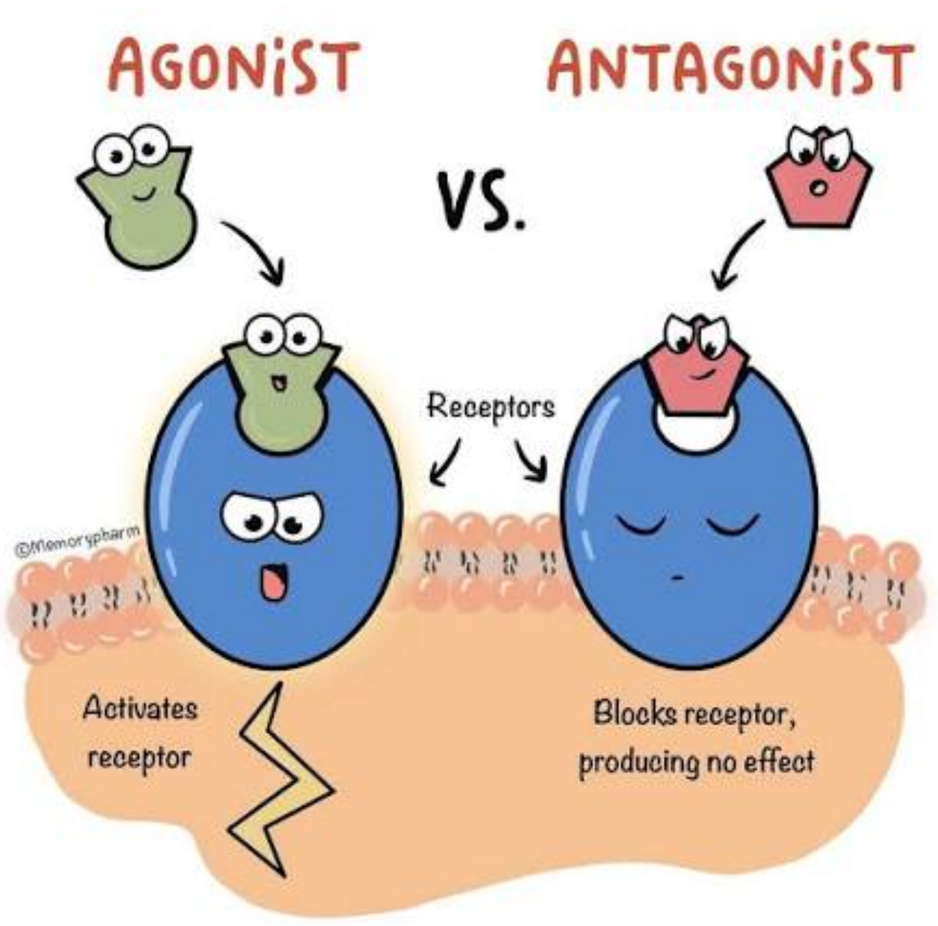
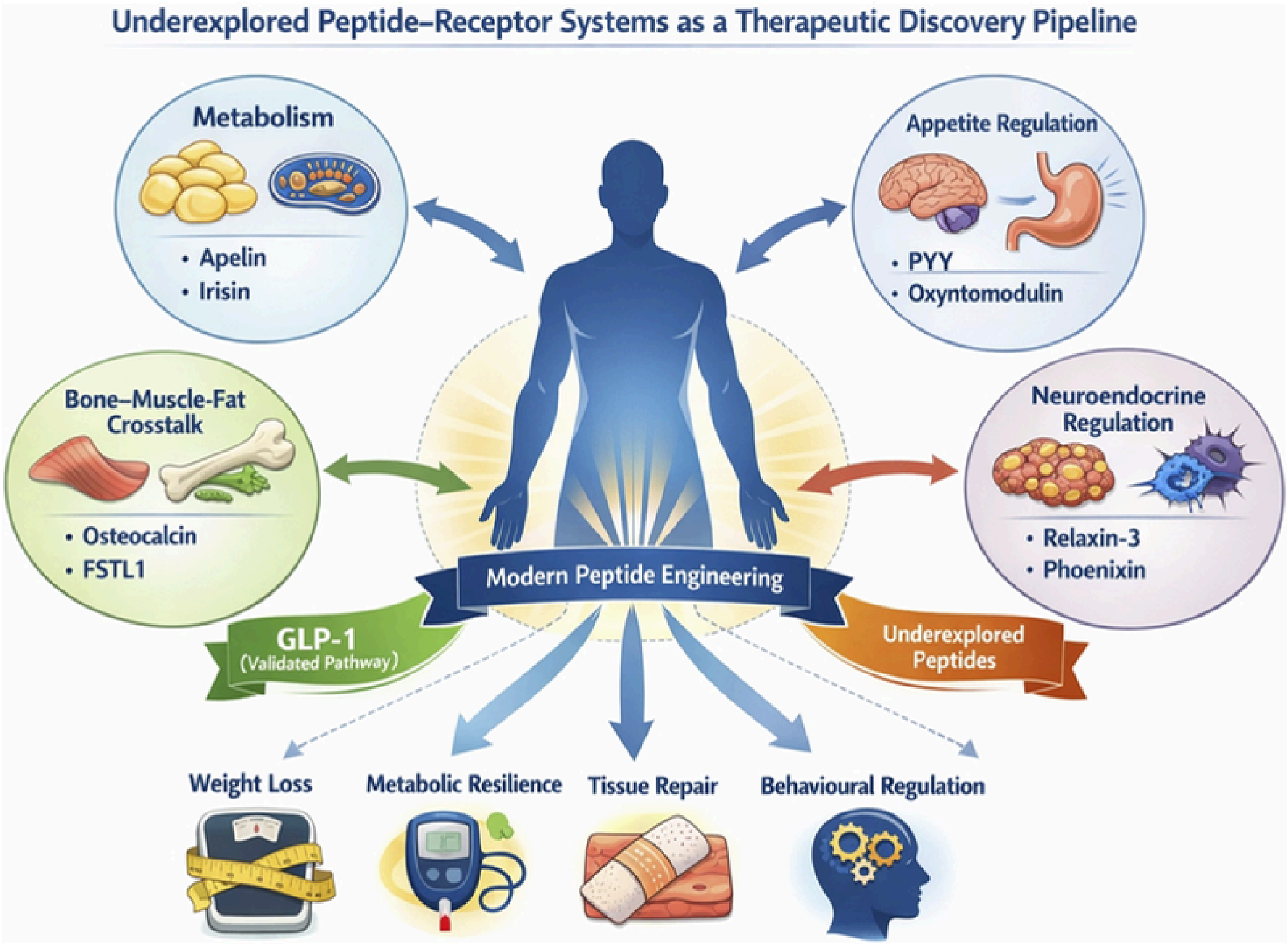


Figure 1.2 — Agonist vs antagonist

Three concepts make this clinically useful:

Agonist vs. antagonist:
An agonist binds a receptor and activates it, mimicking the natural signal. An antagonist binds and blocks it, preventing the natural signal. Most peptides used in aesthetic and metabolic medicine are agonists — they amplify a desired pathway. GLP-1 agonists, melanocortin agonists (PT-141), and GH secretagogues all work by turning a system on.

Receptor distribution explains side effects:
A receptor is rarely found in just one place. GLP-1 receptors sit in the pancreas, stomach, brain, and cardiovascular system — which is why a GLP-1 agonist both suppresses appetite (brain) and causes nausea (delayed gastric emptying). When you know where a peptide's receptors live, its side-effect profile stops being a surprise and becomes predictable. This single principle — map the receptors, anticipate the effects — is one of the most useful clinical habits in the field.



Selectivity is a feature:

An agonist binds a receptor and activates it, mimicking the natural signal. An antagonist binds and blocks it, preventing the natural signal. Most peptides used in aesthetic and metabolic medicine are agonists — they amplify a desired pathway. GLP-1 agonists, melanocortin agonists (PT-141), and GH secretagogues all work by turning a system on.

Mechanism Is a Hypothesis, Not a Result

Here is the caution that will recur throughout this book. A clear, plausible mechanism is necessary but not sufficient evidence that a peptide works in patients.

It is entirely possible — common, even — for a peptide to do exactly what its mechanism predicts at the molecular level and still fail to produce a meaningful clinical outcome. A growth hormone secretagogue may reliably raise GH and IGF-1 (the biomarker moves) without any proven effect on body composition or aging (the outcome that matters). A healing peptide may promote angiogenesis in a petri dish or a rodent and still lack any controlled human trial showing it heals injuries faster.

The gap between *mechanism* and *outcome* is where most peptide hype lives. Understanding how a peptide works tells you what it *might* do. Only human evidence tells you what it *actually* does. Holding those two apart — taking mechanism seriously as a hypothesis while demanding outcome data before believing the promise — is the central discipline of practicing in this field, and the subject of Chapter 3.

Key Takeaways:

- A peptide is a short amino-acid chain (roughly 2–50 residues) that carries a specific biological signal; therapeutic peptides mimic, block, or amplify natural signals.
- Small modifications to a peptide's sequence or structure can dramatically change its potency and half-life; many drugs are engineered analogs of natural peptides.
- Naming is inconsistent (research code, generic, brand), and not everything sold as a "peptide" is one — some are small molecules.
- Peptides are best classified by function (what they do), with route of administration and regulatory status as essential cross-cutting distinctions.
- Most peptides act as receptor agonists; mapping where a receptor is distributed predicts both effects and side effects.
- A plausible mechanism is a hypothesis, not proof. Mechanism tells you what a peptide might do; only human evidence tells you what it actually does.

2



PHARMACOKINETICS: ABSORPTION, HALF-LIFE, AND ROUTES OF DELIVERY

Why Pharmacokinetics Matters for Peptides

Pharmacokinetics is what the body does to a drug — how it absorbs, distributes, metabolizes, and eliminates it. For peptides, this is not academic background; it is the difference between a compound that works and one that never reaches its target in a usable form.

Peptides face a problem small-molecule drugs largely escape: they are made of the same material the body uses for food. The digestive system is built to break proteins and peptides into amino acids, and enzymes throughout the blood and tissues continuously chop circulating peptides apart. Left unmodified, most therapeutic peptides would be degraded within minutes. Nearly every practical question in this field — why a drug is injected rather than swallowed, why it's dosed weekly versus daily, why one analog succeeded where the natural hormone failed — traces back to pharmacokinetics.

Four concepts carry almost all of the clinical weight: **absorption**, **half-life**, **route of delivery**, and **clearance**.

Absorption and Bioavailability

Bioavailability is the fraction of an administered dose that actually reaches systemic circulation in active form. For peptides, this number is often the central design challenge.

Taken orally, most peptides have very low bioavailability — frequently in the low single-digit percentages or less — because stomach acid and digestive enzymes destroy them before absorption. This is why the injectable route dominates the field, and why any oral or topical peptide claim deserves immediate scrutiny:

Does enough of the molecule actually survive to reach its target?

Oral semaglutide (Rybelsus) illustrates both the problem and the workaround. To make an oral GLP-1 viable at all, it is co-formulated with an absorption enhancer and must be taken on an empty stomach with minimal water, then followed by a waiting period before anything else is consumed — and even then its bioavailability is far lower than the injectable version, which is why oral doses are numerically much higher. The elaborate administration ritual exists entirely to claw back a little absorption from a hostile environment.

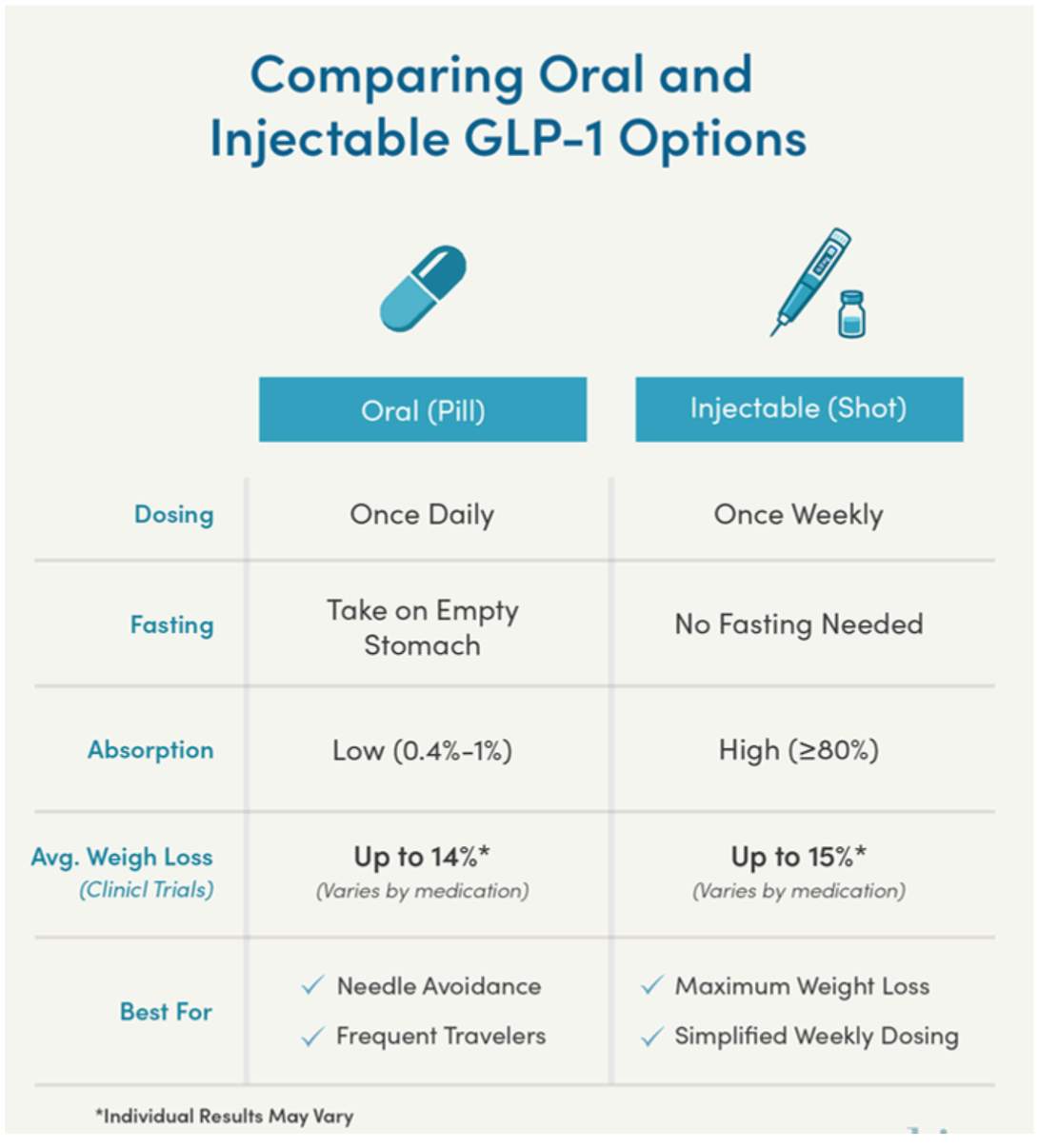


Figure 2.1 — comparing oral and injectable options

Topical peptides face a different barrier: the skin. The stratum corneum is an effective wall, and large or charged molecules cross it poorly. Some skin peptides are engineered specifically to penetrate (for example, palmitoylated or carrier-linked versions), but topical delivery always raises the question of whether the active molecule is reaching the dermis in a meaningful concentration or merely sitting on the surface. This is a recurring theme in the skin chapter: injectable and topical versions of the "same" peptide are not clinically equivalent.

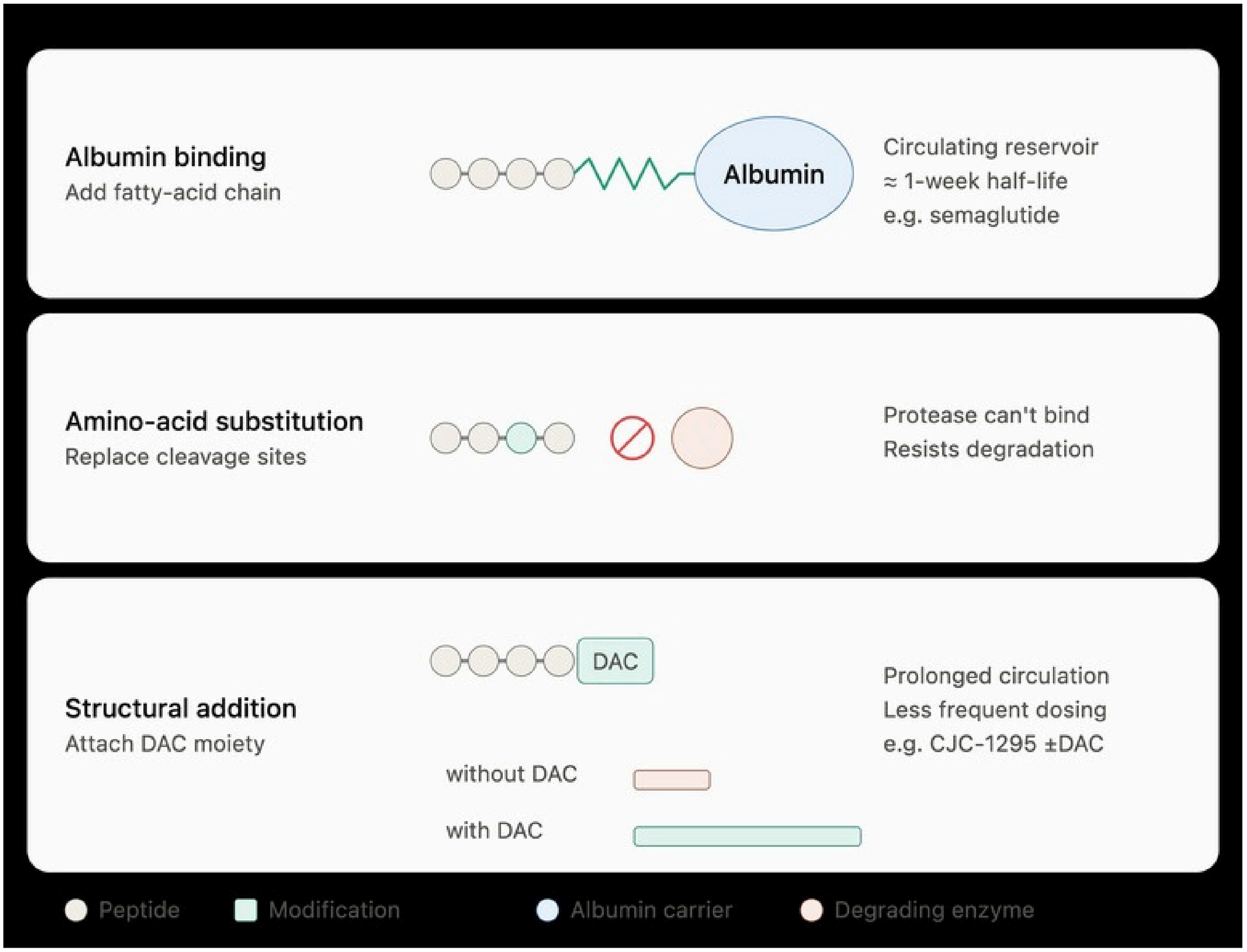
Half-Life: The Engine of Dosing Schedules

A drug's half-life is the time it takes for its plasma concentration to fall by half. It is the single most important determinant of how often a peptide must be dosed, and it explains the entire structure of modern peptide regimens.

Natural peptide hormones tend to have very short half-lives — often minutes — because rapid clearance is how the body keeps hormonal signals precise and pulsatile. That is excellent biology but poor pharmacology: a drug that vanishes in minutes is impractical to administer. The history of therapeutic peptides is largely the history of extending half-life through clever modification.

Several engineering strategies recur:

- **Albumin binding.** Attaching a fatty-acid chain lets the peptide bind albumin, the most abundant blood protein, which



acts as a circulating reservoir that releases the drug slowly. Semaglutide uses this to reach a roughly one-week half-life.

- **Amino-acid substitution.** Replacing the specific residues that enzymes recognize makes the peptide resistant to breakdown.

- **Structural additions (e.g., DAC).** Some analogs add a drug-affinity complex or similar moiety to prolong circulation — the distinction between CJC-1295 "with DAC" and "without DAC" is precisely a half-life difference, and it changes the dosing frequency and the biological effect.

Half-life also shapes safety counseling. A long half-life means a drug lingers long after the last dose — which is why semaglutide must be discontinued well before a planned pregnancy roughly two months, to allow full clearance), and why a long-acting agent's side effects cannot simply be "turned off" by stopping the injection.

A related concept is pulsatile versus sustained signaling, which matters especially for the growth hormone axis. The body naturally releases GH in pulses, particularly at night. A short-acting secretagogue tends to preserve that natural pulse, while a long-acting one (or a sustained small molecule like MK-677) flattens it into a continuous elevation. Whether you want to mimic the natural pulse or override it is a genuine clinical and theoretical question — and one reason "longer-acting" is not automatically "better."

Strategy	How It Works	Effect on Dosing	Example
Albumin binding	Fatty-acid chain binds albumin, creating a slow-release reservoir	Extends to days; enables weekly dosing	Semaglutide (~1-week half-life)
Amino-acid substitution	Replaces residues that enzymes target, resisting breakdown	Prolongs circulation	Many modern analogs
Structural addition (e.g., DAC)	Adds a moiety that slows clearance	Converts short-acting to long-acting	CJC-1295 with vs. without DAC

Table 2.1 — Half-Life Extension Strategies

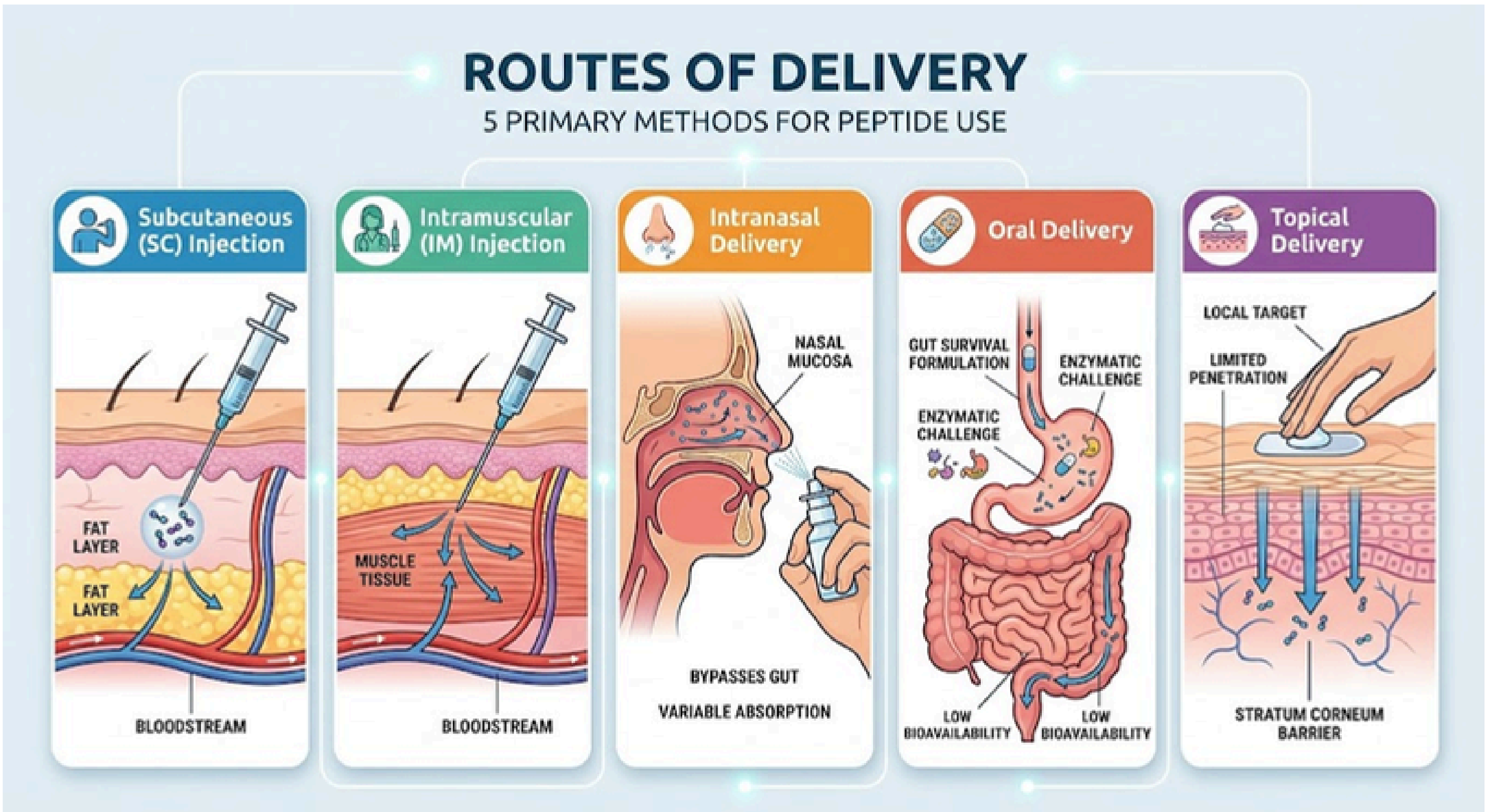
Routes of Delivery

The route determines how much drug arrives, how fast, and how the patient experiences treatment. Five routes account for nearly all peptide use.

- **Subcutaneous (SC)** injection is the workhorse. The peptide is injected into the fat layer just beneath the skin, from which it absorbs steadily into the bloodstream. SC delivery is reliable, self-administrable, and suits the slow, sustained absorption most peptide regimens want.

The overwhelming majority of peptides in this book are given this way.

- **Intramuscular (IM)** injection delivers into muscle, generally producing faster absorption than SC. It is less common for routine peptide therapy and is usually reserved for specific formulations or protocols.
- **Intranasal** delivery suits certain peptides that act centrally and can cross the nasal mucosa — semax and selank are typically administered this way. The nasal route bypasses the gut, but absorption is variable and dosing is less precise than injection.



- **Topical** delivery is used for skin peptides, where the target is local rather than systemic. The clinical question is always penetration: a topical peptide that cannot cross the stratum corneum may have cosmetic-surface effects at best, regardless of its theoretical mechanism.

When a single peptide is available in more than one route, the routes are rarely interchangeable. Different bioavailability, different effective dose, different onset — treat each formulation as its own entity.

Route	Typical Bioavailability	Onset / Absorption	Best Suited For	Key Limitation
Subcutaneous (SC)	Good, reliable	Slow, sustained	Most peptide therapy; self-injection	Requires injection; technique-dependent
Intramuscular (IM)	Good	Faster than SC	Specific formulations/protocol	Less convenient; more discomfort
Intranasal	Variable, often low	Rapid but inconsistent	Centrally-acting peptides (semax, selank)	Imprecise dosing; absorption varies
Oral	Very low (often <5%)	Slow; gut-dependent	Only specially formulated peptides	Enzymatic destruction; rigid administration rules
Topical	Low; penetration-limited	Local, gradual	Skin-targeted peptides	Stratum corneum barrier; may not reach dermis

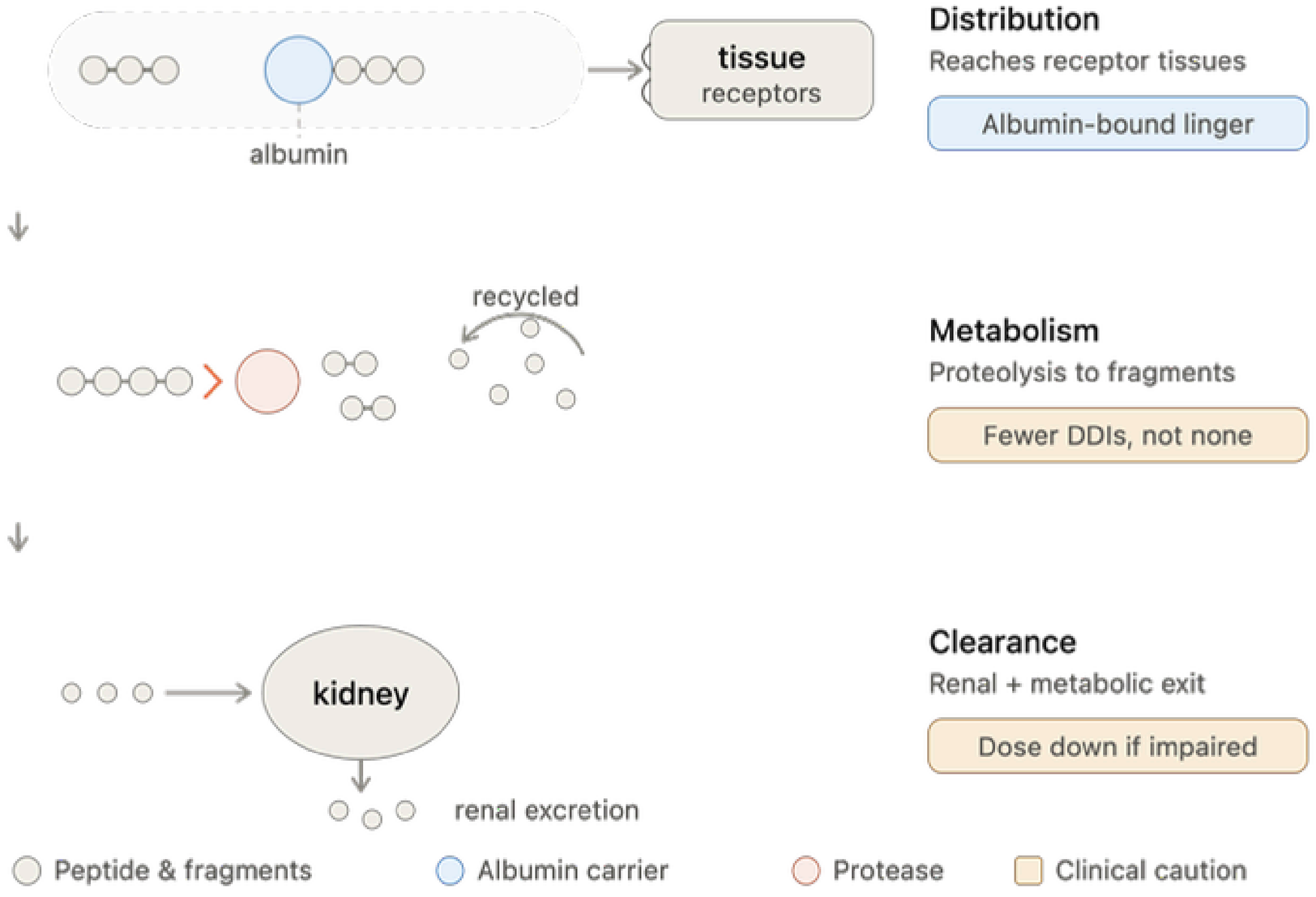
Table 2.2 — Routes of peptide delivery at a glance

Distribution, Metabolism, and Clearance

Once absorbed, a peptide distributes through the body, reaching the tissues where its receptors live. Distribution is shaped by size, charge, and protein binding; albumin-bound peptides, for instance, stay in circulation longer and distribute differently than free ones.

Metabolism for peptides is mostly **proteolysis** — enzymatic cleavage into smaller fragments and ultimately amino acids, which the body recycles. Unlike many small-molecule drugs, peptides generally do not depend heavily on the liver's cytochrome P450 system, which means classic drug–drug interactions through that pathway are less of a concern. This is a genuine advantage, but it does not make peptides interaction-free — pharmacodynamic interactions (for example, a GLP-1 agonist plus insulin or a sulfonylurea raising hypoglycemia risk, covered in Chapter 9) remain very real.

Clearance — elimination from the body — occurs through metabolic breakdown and, for many peptides and their fragments, renal excretion. Reduced kidney function can therefore prolong exposure to some peptides or their active metabolites, a consideration in patients with chronic kidney disease. As a general principle, impaired clearance means a drug and its effects last longer than expected, which argues for caution and conservative dosing in renal or hepatic impairment.



Putting It Together: Reading a Peptide's Pharmacokinetics

For any peptide, a practitioner can ask a short, structured set of questions that predict most of its practical behavior:

- **How is it given**, and what is the bioavailability of that route? This tells you whether the dose on the label is actually reaching the bloodstream.
- **What is its half-life?** This sets the dosing frequency and tells you how long effects — and side effects — will persist after stopping.
- **Is the signal pulsatile or sustained**? Especially for the GH axis, this shapes both the expected effect and the theoretical risk.
- **How is it cleared, and is the patient's clearance impaired?** Renal or hepatic dysfunction can turn a standard dose into an excessive one.

These four questions, applied consistently, let you reason about a peptide's behavior even when detailed data is sparse — which, for many of the compounds in this field, it is.

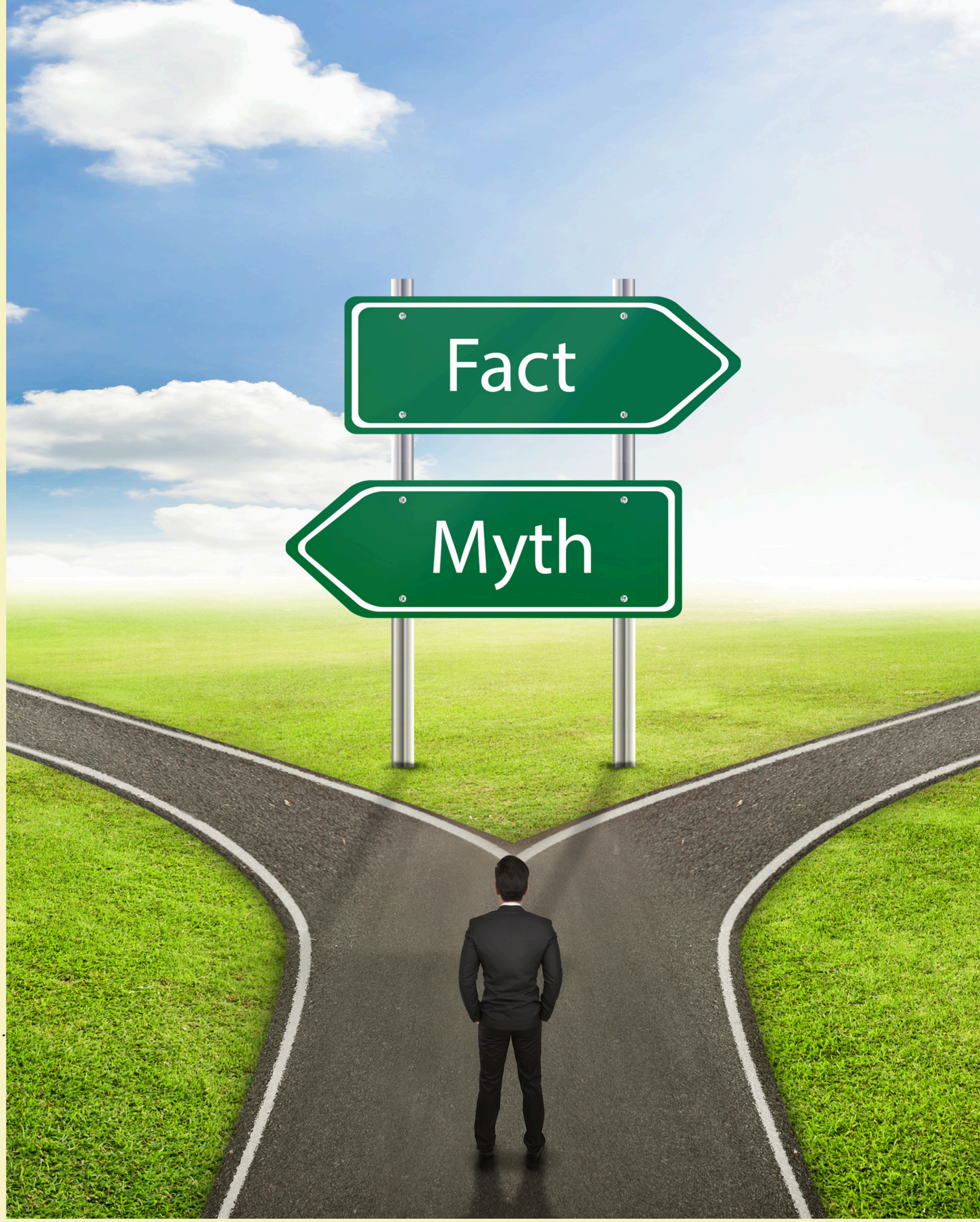
Question	What It Tells You	Why It Matters Clinically
What route, and what bioavailability?	How much active drug actually reaches circulation	A high label dose may still deliver little drug (oral/topical)
What is the half-life?	How often to dose; how long effects persist	Long half-life lingers after stopping (e.g., pre-pregnancy washout)
Pulsatile or sustained signaling?	Whether it mimics or overrides natural rhythm	Especially for GH axis; "longer" isn't automatically "better"
How is it cleared? Is clearance impaired?	Duration of exposure	Renal/hepatic impairment can make a standard dose excessive

Table 2.3 — The 4 PK questions for any peptide

Key Takeaways:

- Peptides are vulnerable to enzymatic and digestive breakdown, which makes pharmacokinetics the central practical challenge of the field.
- Oral bioavailability is typically very low; injection dominates, and any oral or topical claim should prompt the question of whether enough active drug reaches the target.
- Half-life governs dosing frequency and is usually extended by engineering (albumin binding, amino-acid substitution, structural additions); a long half-life means effects persist well after the last dose.
- Subcutaneous injection is the default route; intranasal, oral, and topical routes each carry absorption trade-offs, and different routes of the same peptide are not interchangeable.
- Peptides are metabolized mainly by proteolysis and cleared partly by the kidneys; they largely avoid CYP450 interactions but not pharmacodynamic ones, and impaired clearance prolongs their effect.
- Four questions — route/bioavailability, half-life, pulsatile vs. sustained, and clearance — let you predict most of a peptide's clinical behavior.

3



READING THE EVIDENCE: TRIAGING ANY PEPTIDE FROM PROVEN TO HYPE

The Most Important Skill in the Book

New peptides appear faster than anyone can study them. Patients will bring you compounds this handbook does not cover, and the field will have invented new ones by the time you read this. Memorizing a fixed list is therefore a losing strategy. The durable skill — the one that protects you and your patients regardless of what's trending — is evidence triage: the ability to take any peptide, known or unknown, and rapidly place it on a spectrum from genuinely proven to pure marketing.

This chapter teaches that skill. Everything in Part II is an application of it.

The Evidence Spectrum

Every peptide lives somewhere on a single scale defined by the quality of its human evidence.

The tiers are not permanent. A peptide can move *toward proven* as trials are completed, or *toward hype* as promising mechanisms fail in humans. The point is not to memorize the placements but to learn the questions that produce them.

The Hierarchy of Evidence

Not all "studies" are equal. When a seller cites "clinical research," the first question is what kind. From weakest to strongest:

Most gray-market peptides sit at levels 1–3 while being marketed as though they were at level 5. The single most clarifying move you can make is to ask, for any claimed benefit: *is there a randomized, controlled human trial showing this outcome — not a biomarker, the actual outcome?*

Biomarker vs. Outcome: The Central Trap

This distinction deserves its own emphasis because it is where most sophisticated-sounding hype hides.

A **biomarker** is a measurable signal — IGF-1 rose, a receptor activated, angiogenesis increased in tissue. An **outcome** is a result the patient actually cares about — they healed faster, lost weight, lived longer, looked better. A peptide can reliably move a biomarker and produce *no meaningful outcome at all.*

A growth hormone secretagogue that raises IGF-1 has moved a biomarker; whether it improves body composition or slows aging is a

separate, often unproven question. "It raises your growth hormone" is true and irrelevant if raising growth hormone doesn't deliver the promised result. Train yourself to hear a biomarker claim and immediately ask: and does that translate into an outcome that's been demonstrated in humans?

A Practical Triage Checklist

For any peptide a patient or supplier puts in front of you, run these questions:

1. **What is the claimed outcome?** (Not the mechanism — the actual benefit.)
2. **What human evidence supports that outcome?** Where does it sit on the hierarchy above?
3. **Is the evidence about an outcome, or just a biomarker?**
4. **What is its regulatory status?** (Chapter 4 — approved, compounded, or gray-market.)
5. **What is the risk profile, including the unknowns?**

Tier	What Defines It	What It Means for You	Examples
Proven	Strong randomized human trials; FDA approval for the indication	Prescribe with confidence within the approved use	Semaglutide, tirzepatide, tesamorelin (its indication), PT-141 (its indication)
Plausible	Real mechanism; some human data, but limited, small, or non-rigorous	Use with caution, full disclosure, and documentation	CJC-1295 + ipamorelin, thymosin α-1
Hype	Marketing claims resting on animal/cell data or none; no quality human trials	Recognize, counsel honestly, generally avoid	AOD-9604, MOTS-c, epitalon, 5-Amino-1MQ

Table 3.1 — The Evidence Spectrum

If the honest answers are "impressive mechanism, mostly animal data, biomarker-only, not approved, unknown long-term risk," you are looking at a hype-tier compound — regardless of how confident the marketing is. Saying so to a patient, clearly and kindly, is a mark of expertise, not ignorance.

Key Takeaways:

The durable skill is triage, not memorization: place any peptide on the proven–plausible–hype spectrum using its human evidence.

- Evidence has a hierarchy; in-vitro and animal data sit at the bottom, RCTs and systematic reviews at the top. Much hype is level-1–3 data sold as level-5.
- Distinguish biomarkers (a number moved) from outcomes (the patient benefited). A moved biomarker is a hypothesis, not a result.
- Run every peptide through five questions: claimed outcome, supporting human evidence, biomarker-vs-outcome, regulatory status, and risk.

Level	Type	Weight	The Catch
1	In vitro (cell/petri dish)	Lowest	A molecule's behavior in a dish rarely predicts its effect in a person
2	Animal studies	Low	Rodents are not humans; most compounds that work in mice fail in people
3	Case reports / uncontrolled series	Low–moderate	No control group means no way to separate drug effect from placebo or natural course
4	Small or non-blinded human trials	Moderate	Vulnerable to bias; promising but not definitive
5	Randomized, double-blind, placebo-controlled trials (RCTs)	High	The gold standard; isolates the drug's true effect
6	Systematic reviews / meta-analyses	Highest	Synthesizes all quality evidence; hardest to argue with

Table 3.2 — Strength of Evidence, Weakest to Strongest

4



THE REGULATORY LANDSCAPE: FDA STATUS, 503A VS. 503B, CATEGORY 2, AND THE GRAY MARKET

Why This Chapter Governs All the Others

A peptide's biology and its legality are entirely separate questions. A compound can be scientifically promising and still be illegal for you to prescribe. Clinical efficacy is answered by trials; legal permissibility is answered by FDA status, pharmacy classification, and current enforcement. **Both must be satisfied before you prescribe** — and most clinicians only ever check the first. This chapter covers the second.

A foundational warning: regulatory status is a snapshot, not a fact. It changes — sometimes within months — driven not by new science but by new determinations, shortage listings, and enforcement. Treat every specific status in this book as a starting point for verification, not a settled answer.



The Two Compounding Pathways

When a drug isn't available as a standard FDA-approved product, it may be compounded — prepared by a pharmacy. Two legal pathways exist, and they are not interchangeable.

Feature	503A (Traditional Pharmacy)	503B (Outsourcing Facility)
Who it serves	Individual patient, specific prescription	Batches, no patient-specific Rx required
Scale	One patient at a time	Oversight
Oversight	Primarily state boards of pharmacy	FDA-registered and inspected
Standards	USP standards; approved components	cGMP (manufacturer-grade)
Distribution	To the prescribing patient	Substance bar
Substance bar	Approved components / USP monograph	Higher bar for eligibility

Table 4.1 — 503A vs. 503B

The practical takeaway: 503B facilities operate under manufacturer-level scrutiny, which generally makes them a higher-assurance source; 503A pharmacies serve individualized needs but vary widely in quality, which is why the certificate-of-analysis discipline in Chapter 5 matters.

The Compounding Gate

Before any bulk substance can be legally compounded by either pathway, it must clear a regulatory gate. It qualifies only if it is one of the following: a component of an FDA-approved drug, listed on the FDA's bulk substances list as allowable, or the subject of an official USP monograph. **If a substance is on none of these pathways, compounding it is not legally permissible — no matter how popular or widely used it is.** Many peptides circulating in clinics have never cleared this gate. Widespread use is not the same as legal use.

Category 2: "Do Not Compound"

When the FDA evaluates a bulk substance for compounding eligibility, it can assign categories. The one to know is Category 2: substances the agency has flagged with safety

concerns that preclude compounding. This is not a gray area or a technicality — it is an explicit determination that a substance should not be compounded, and it carries real enforcement risk. Several peptides that became popular in clinical practice — including BPC-157, TB-500, CJC-1295, and ipamorelin — have been placed in, or proposed for, Category 2 review.

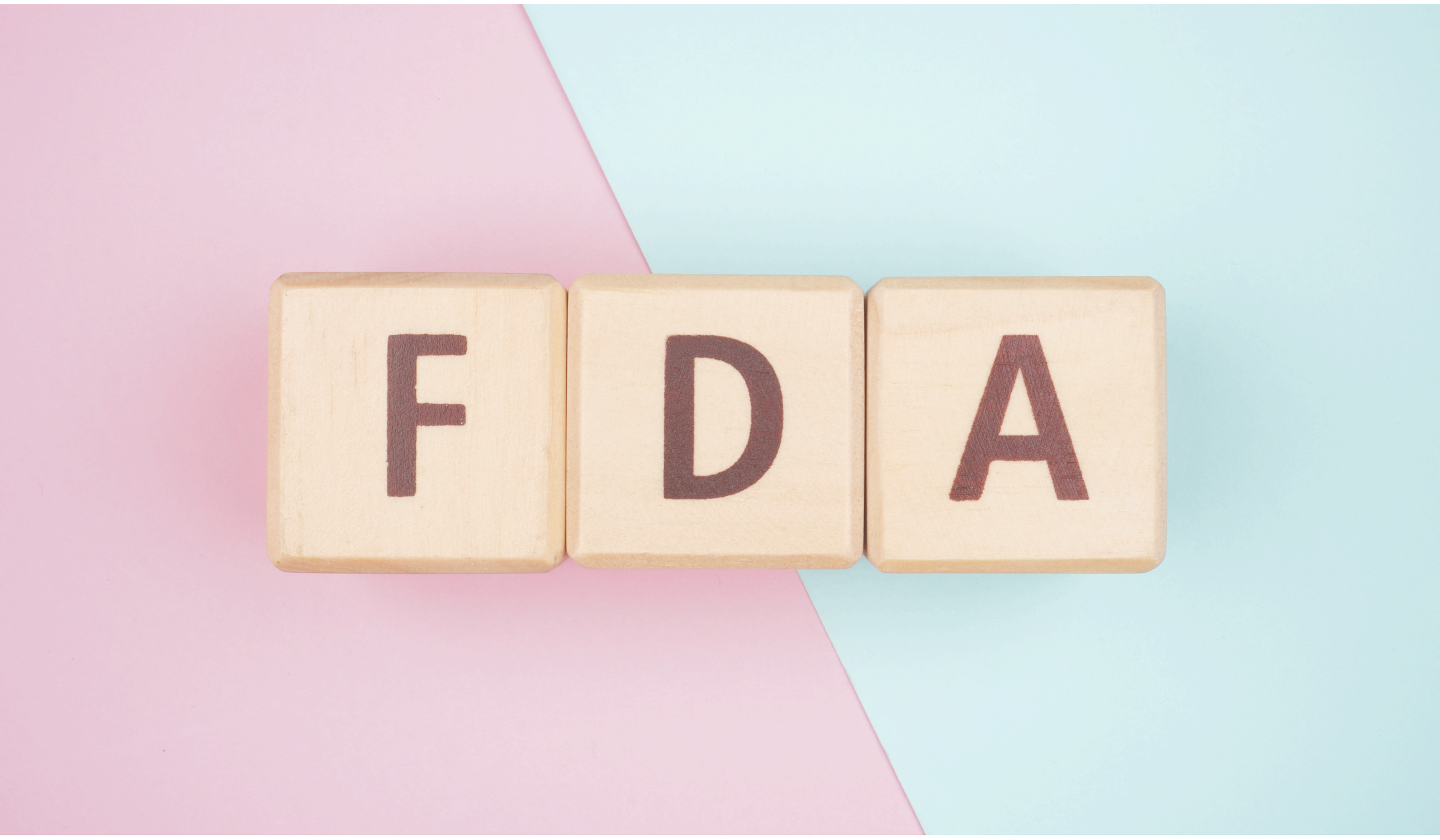
Popularity is not a legal defense.

Case Study: The GLP-1 Saga

The clearest illustration of how fast this landscape moves is the recent history of compounded semaglutide and tirzepatide.

Period	What Happened
2021	Semaglutide and tirzepatide approved; demand outpaces supply
2022	FDA places them on the drug shortage list → compounding temporarily permitted
2022–2023	Hundreds of pharmacies compound at scale; prices fall; quality varies; adverse events reported
Late 2024	Tirzepatide shortage declared resolved → exemption begins to close
2025	Semaglutide shortage resolved → compounding of both becomes legally precarious
2026	FDA proposes barring bulk compounding of semaglutide, tirzepatide, liraglutide (not finalized as of this writing)

Table 4.2 — The GLP-1 Compounding Timeline



The lesson: a compound that was routine to prescribe in one year became a source of legal exposure in the next — without any change in the science. Verify status at the time of every prescription, not once.

The Gray Market and "Research Use Only"

A large volume of peptides is sold online labeled "Research Use Only — Not for Human Use." This phrase is not a safety designation; it is a legal workaround that lets sellers move unregulated chemicals while avoiding FDA oversight. Prescribing, recommending, or directing patients to these products exposes you to serious professional and legal liability regardless of what the label says.

What that label really means: no purity testing, no sterility or endotoxin standards, no manufacturing oversight, no adverse-event reporting, and no recourse if something goes wrong. Impurities, mislabeling, and contamination in these products are documented, not hypothetical.

The Clinician's Regulatory Playbook

Rule	In Practice
Default to approved	Start with the FDA-approved product; compounding is the exception
Interrogate the pharmacy	503A or 503B? On the bulks list? Last inspected when?
Demand a Certificate of Analysis	Every batch, from an independent third-party lab
Never say "identical"	Compounded ≠ FDA-approved equivalent; don't represent it as such
Re-verify status	Check current status before each prescribing cycle

Table 4.3 — Five Rules That Protect Your License

Key Takeaways:

- Efficacy and legality are separate questions; both must be satisfied before prescribing.
- 503A (patient-specific, state-overseen) and 503B (batch, FDA-inspected, cGMP) are distinct pathways; every compounded substance must also clear the bulks gate.
- Category 2 means "do not compound" — an explicit safety determination, not a technicality; several popular peptides are implicated.
- Legal status is a snapshot: the GLP-1 saga shows a compound can go from routine to precarious without any change in science. Verify every time.
- "Research Use Only" is a legal loophole, not a safety label; directing patients to gray-market products is a serious liability.

5



SOURCING, RECONSTITUTION, DOSING MATH, AND INJECTION TECHNIQUE

From Vial to Patient

The safest prescription can still harm a patient if the product is poor, the reconstitution is wrong, the math is off, or the injection is unsafe. This chapter covers the physical chain of custody — the practical mechanics that turn an order into a dose.

Sourcing and the Certificate of Analysis

Your single most important quality document is the Certificate of Analysis (CoA) — a lab report verifying what is actually in the vial. Demand one for every batch, from an independent third-party lab, not the compounder's own testing.

Parameter	What to Check	Why
Identity	Is it the correct molecule?	Confirms you have what was ordered
Purity	Typically aim for ≥98%; review named impurities	Impurities drive adverse events
Sterility & endotoxin	Required for any injectable	Contamination risk is real
Confirmation method	HPLC / mass spec	Validates the identity and purity claims
Lot number	Matches the vial in hand	Ties the document to the actual product

Table 5.1 — How to Read a Certificate of Analysis

Sourcing red flags: no CoA (or only in-house testing), "research use only" labeling, prices far below market, unclear 503A/503B status, or claims of being "identical" to a brand-name drug.

Reconstitution

Most peptides arrive lyophilized (freeze-dried powder) and must be dissolved before use. Done wrong, this degrades the peptide or contaminates the vial.

Diluent choice: Bacteriostatic water (containing 0.9% benzyl alcohol) resists microbial growth and is preferred for multi-dose vials used over days or weeks. Sterile water has no preservative and suits single-use or very short windows only. Never use tap water or, unless specified, saline.

The golden rule: aim the water stream slowly down the inside wall of the vial — never spray it directly onto the powder, and never shake. Force and foaming shear the peptide and destroy potency. Swirl gently or let it dissolve on its own, and wait until the solution is fully clear before drawing a dose.

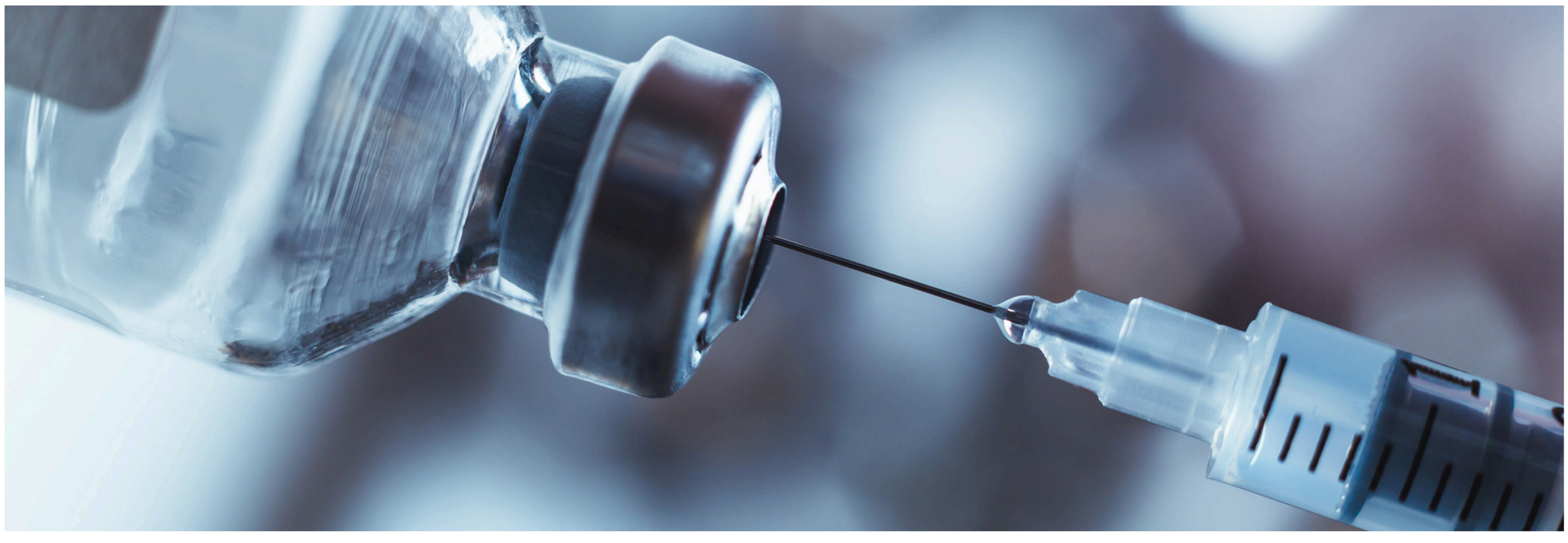
Always label the reconstituted vial with the drug, the concentration, and the date — because the concentration you create is the input for all dosing math, and an unlabeled vial is a dosing error waiting to happen.

Dosing Math

This is where arithmetic becomes the most dangerous step. Three formulas govern everything:

- Concentration (mg/mL) = peptide (mg) ÷ water added (mL)
- Volume to draw (mL) = dose ÷ concentration
- Units on an insulin syringe = volume (mL) × 100 (because 1 mL = 100 units)

Worked example: A 5 mg vial reconstituted with 2 mL of bacteriostatic water gives 2.5 mg/mL, or 2,500 mcg/mL. To give a 250 mcg dose: 250 ÷ 2,500 = 0.1 mL → ×100 = 10 units.



Water Added	Concentration	Volume to Draw	Units
1 mL	5,000 mcg/mL	0.05 mL	5 units
2 mL	2,500 mcg/mL	0.10 mL	10 units
5 mL	1,000 mcg/mL	0.25 mL	25 units

Table 5.2 — Same Dose, Different Reconstitution (5 mg vial, 250 mcg dose)

The table makes the central hazard visible: the same dose is a different number of units depending only on how the vial was reconstituted. This is why labeling the vial and recording its concentration is non-negotiable. The classic catastrophic error is a 10× slip — confusing units with mL, or misreading the concentration — so sanity-check every draw against the prior dose; if the number suddenly looks very different, recheck the math before injecting.

Injection Technique

Almost all peptides are given subcutaneously, into the fat layer just under the skin, using an insulin syringe (typically 29–31 gauge, 8–13 mm). The reliable, sustained absorption of the SC route suits most regimens.

Sites: abdomen (at least two inches from the navel), outer thigh, upper outer buttock, and back of the upper arm. Pinch a fold of fat to ensure subcutaneous, not intramuscular, placement, and insert at 45–90° (90° with adequate fat, 45° if lean).

Rotate sites every injection. Repeated injection into the same spot causes lipohypertrophy — lumps that absorb erratically and undermine dosing consistency.

Safety essentials: alcohol-wipe the stopper and the site each time, use a fresh sterile needle for every injection, never recap a used needle by hand, and dispose of needles in an FDA-cleared sharps container. One vial, one patient — never share.

Patient self-injection should be taught by demonstration followed by teach-back, with written instructions, a rotation map, a sharps container, and clear "call us / go to the ER" guidance, since most patients inject at home.

Teach home-injecting patients with demonstration, teach-back, written instructions, and clear escalation guidance.

Key Takeaways:

- The Certificate of Analysis is your core quality safeguard: demand one per batch from an independent lab, and know how to read identity, purity, sterility, and lot number.
- Most peptides are lyophilized and require careful reconstitution: bacteriostatic water for multi-dose use, stream down the wall, never shake, and always label the concentration.
- Three formulas run all dosing: concentration = mg ÷ mL, volume = dose ÷ concentration, units = mL × 100. The same dose changes units with reconstitution volume — label vials and sanity-check every draw.
- Inject subcutaneously with a fresh needle, rotate sites to prevent lipohypertrophy, and dispose of sharps safely.

Part I I

The Peptides



A Note on the Monograph Format

Every peptide in Part II follows the same structure so you can find what you need quickly and compare across compounds:

- **Status** — FDA status · regulatory/compounding category · anti-doping (WADA)
- **Mechanism** — how it works, briefly
- **Evidence** — what the human data actually shows
- **Dosing** — approved regimens where they exist; clearly labeled reference (non-approved) ranges where they don't
- **Monitoring** — what to track
- **Cautions** — contraindications and red flags
- **Counseling** — what to tell the patient
-

All status and dosing information is a snapshot — verify current status before prescribing.



6



SKIN AND ANTI-AGING PEPTIDES

Overview

Skin peptides are the most familiar — and most overhyped — corner of the field, because they sit at the intersection of medicine and cosmetics. Most are sold as topical cosmetic ingredients rather than approved drugs, which means two things: they reach the market without drug-level efficacy trials, and their real-world effect is governed less by their elegant mechanisms than by a blunt physical fact: *can the molecule actually cross the skin barrier?*

It helps to group skin peptides by how they're meant to work:

A recurring theme across all three: topical and injectable versions of the same peptide are not equivalent. Topical delivery must fight the stratum corneum; injectable/compounded delivery bypasses it but moves the peptide out of the well-trodden cosmetic world and into the regulatory gray zone covered in Chapter 4.

Class	What They Do	Example
Signal peptides (matrikines)	Tell fibroblasts to produce more collagen/elastin	Matrixyl (palmitoyl pentapeptide-4)
Carrier peptides	Deliver a trace mineral cofactor (copper) that drives repair enzymes	GHK-Cu (copper tripeptide-1)
Neurotransmitter-inhibiting peptides	Mimic Botox by dampening muscle-contraction signaling	Argireline (acetyl hexapeptide-8)

Table 6.1 — Three Functional Classes of Skin Peptides

GHK-Cu (Copper Tripeptide-1)

Status: Not an FDA-approved drug. Widely sold as a topical cosmetic ingredient. Injectable/compounded forms are not FDA-approved. Not specifically WADA-prohibited for topical cosmetic use; verify before any injected use in a tested athlete.

Mechanism: A naturally occurring copper-binding tripeptide whose levels decline with age.

It delivers copper — a cofactor for repair enzymes — and signals collagen and elastin synthesis, acts as an antioxidant and anti-inflammatory, modulates matrix metalloproteinases (the enzymes that break down collagen), and promotes angiogenesis. It has a genuine pedigree in wound healing.

Evidence: The best-supported of the skin peptides. In-vitro and animal data are robust, and several small human topical studies report improved skin firmness, reduced fine lines, and better texture. The trials are small and cosmetic-grade rather than large RCTs, so the effect is best described as real but modest — not transformative.

Dosing: Topical (cosmetic): serums and creams, commonly in the ~1–2 mg/mL (roughly 0.1–0.2%) range, applied once or twice daily. Reference (non-approved), injectable/microneedling-adjunct: low-concentration compounded solutions are used in some clinics; there is no established, approved protocol — included for recognition, not endorsement.

Monitoring: Topical use needs little beyond watching for local irritation. For any injected/compounded use, apply the sourcing and CoA discipline from Chapter 5.

Cautions: Generally well tolerated topically; possible local irritation or contact sensitivity. Avoid layering directly with strong actives (e.g., high-strength vitamin C) that may destabilize the copper complex.



Matrixyl (Palmitoyl Pentapeptide-4)

Status: Not an FDA-approved drug. Sold as a topical cosmetic ingredient. Not a WADA concern in topical cosmetic use.

Mechanism: A matrikine — a fragment of type I collagen (the "KTTKS" sequence) attached to a palmitoyl (fatty-acid) chain to help it penetrate skin. It mimics the signal the body produces when collagen breaks down, prompting fibroblasts to synthesize new collagen and extracellular matrix. The related "Matrixyl 3000" blends palmitoyl tripeptide-1 and palmitoyl tetrapeptide-7.

Evidence: Small topical cosmetic studies show modest reductions in wrinkle depth and improved skin appearance over weeks to months; some compared it favorably to low-dose retinol. Evidence is cosmetic-grade and limited — modest, gradual benefit is the honest framing.

Dosing: Topical (cosmetic) only: incorporated into serums/creams, applied once or twice daily; commercial formulations are pre-diluted to manufacturer-recommended use levels. There is no injectable or systemic role.
Monitoring: Minimal; watch for local irritation.
Cautions: Very well tolerated; occasional mild irritation. The main "risk" is overpromising — patients primed by marketing may expect results that topical peptides don't deliver.

Counseling: "It nudges your skin to make more collagen over time. Think of it as a supportive ingredient in a routine, not a standalone fix — results are subtle and build slowly."

Argireline (Acetyl Hexapeptide-8)

Status: Not an FDA-approved drug. Sold as a topical cosmetic ingredient ("topical Botox" in marketing). Not a WADA concern topically.

Mechanism: Mimics a segment of the SNAP-25 protein and competes within the SNARE complex that enables neurotransmitter release at the neuromuscular junction. The intended result is slightly reduced muscle contraction and therefore softened expression lines — conceptually similar to botulinum toxin, but far weaker and entirely topical.

Evidence: Small studies show modest reductions in the depth of expression wrinkles with regular topical use. The effect is real but substantially less than injectable neuromodulators, and is limited by how little peptide actually penetrates to reach the relevant nerves. The "topical Botox" framing oversells it.

Other Notable Skin Peptides

These appear in cosmetic formulations and patient questions; all are topical cosmetic ingredients with modest, mechanism-driven rationale and limited rigorous human data.

Peptide	Class	Claimed Action	Evidence Note
SNAP-8 (acetyl octapeptide-3)	Neurotransmitter-inhibiting	Argireline-type expression-line softening	Modest; topical, penetration-limited
Palmitoyl tripeptide-1	Signal (matrikine)	Collagen support	Cosmetic-grade; often combined
Palmitoyl tetrapeptide-7	Signal	Anti-inflammatory, soothing	Cosmetic-grade; in Matrixyl 3000
Copper peptide variants	Carrier	Repair, antioxidant	Less studied than GHK-Cu

Table 6.2 — Additional Skin Peptides at a Glance

The Honest Verdict on Skin Peptides

Skin peptides are the gentlest, lowest-risk category in this book — and also the one where the gap between marketing and evidence is widest, though here it usually inflates cosmetic benefit rather than promising anything dangerous. The realistic clinical posture: topical peptides (especially GHK-Cu and the matrikines) are reasonable, well-tolerated supportive ingredients that produce modest, gradual improvement; they are not substitutes for the better-proven anti-aging tools (sun protection, retinoids, and, for dynamic lines, injectable neuromodulators). Injectable or compounded skin peptides leave the relatively safe cosmetic world and inherit all the sourcing and regulatory cautions of Chapters 4 and 5. The practitioner's job here is mostly expectation management: offer them honestly as adjuncts, and don't let a patient mistake a peptide serum for a procedure.

Key Takeaways:

- Most skin peptides are topical cosmetic ingredients, not approved drugs; their real-world effect is limited as much by skin penetration as by mechanism.
- Three functional classes: signal peptides/matrikines (Matrixyl), carrier peptides (GHK-Cu), and neurotransmitter-inhibiting peptides (Argireline).
- GHK-Cu is the best-supported, with modest human topical evidence for firmness and fine lines; Matrixyl offers modest gradual wrinkle improvement; Argireline softens expression lines but is not a Botox substitute.
- Topical and injectable/compounded versions are not equivalent — injectable forms carry full gray-market sourcing and regulatory risk.
- The clinical role is supportive and adjunctive; the main skill is honest expectation-setting.



7



HAIR RESTORATION PEPTIDES

Overview

Hair restoration is a high-demand, high-frustration field, and peptides have entered it as both legitimate adjuncts and marketing vehicles. The honest framing up front: no peptide is a first-line, FDA-approved treatment for hair loss.

This chapter covers the true peptides in monograph form and addresses the biologic/procedural adjuncts briefly, since patients routinely ask how they compare.

The proven backbone of androgenetic alopecia treatment remains minoxidil, finasteride, and procedural options; peptides are best understood as adjuncts layered onto that backbone, or as ingredients in combination products, rather than as standalone cures.

It helps to separate what's actually being discussed under "hair peptides," because the category blends three different things:

Category	Examples	Role
True peptides repurposed for hair	GHK-Cu, PTD-DBM	Adjuncts; modest mechanistic rationale
Peptide-adjacent biologics & procedures	PRP, exosomes	Procedural adjuncts; variable evidence
Proven non-peptide standards	Minoxidil, finasteride	First-line; the comparison everything else is measured against

Table 7.1 — What "Hair Peptides" Actually Refers To

GHK-Cu (Copper Tripeptide-1) — for Hair

Status: Not FDA-approved for hair loss. Sold as a topical cosmetic ingredient and in compounded hair formulations.

Mechanism: The same copper-binding tripeptide covered in Chapter 6, applied to the scalp. Proposed hair-specific actions include improving the perifollicular environment through angiogenesis (better blood supply to the follicle), reducing inflammation, modulating the matrix around the follicle, and possibly prolonging the anagen (growth) phase. The rationale is plausible and overlaps with its wound-healing biology.

Evidence: Considerably weaker for hair than for skin. Most support is mechanistic and preclinical, with limited human data — often as one ingredient within multi-component scalp products, which makes it impossible to isolate GHK-Cu's specific contribution. Plausible adjunct, not a proven hair-growth agent.

Dosing: Topical/scalp (cosmetic or compounded): incorporated into serums and scalp solutions at low concentrations, applied daily; frequently combined with minoxidil or other actives. Reference (non-approved), injected/microneedling-adjunct: used in some clinics alongside microneedling; no established, approved protocol — included for recognition only.

Monitoring: Watch for scalp irritation or contact sensitivity; otherwise minimal for topical use. Apply sourcing/CoA discipline (Chapter 5) to any compounded injectable.

Cautions: Generally well tolerated topically. Avoid destabilizing combinations (e.g., simultaneous high-strength vitamin C). Injected forms inherit gray-market quality risk.

Counseling: "It may support the scalp environment and works best alongside proven treatments like minoxidil — not instead of them. Expect a supportive role, and give it months, not weeks."

PTD-DBM (Peptide for Wnt Pathway Activation)

Status:Not FDA-approved. Experimental/ research-stage. Sold in the gray market and in some compounded scalp formulations. Not an established clinical therapy. Verify WADA status before use in tested athletes.

Mechanism: A peptide designed to activate the Wnt/β-catenin signaling pathway, which is involved in hair-follicle regeneration and the induction of new follicles. By interfering with a protein (CXXC5) that normally inhibits Wnt signaling, PTD-DBM is proposed to "release the brake" on follicle regeneration. It is frequently discussed in combination with the Wnt-active compound valproic acid in experimental contexts.

Evidence: Early and largely preclinical — animal models and laboratory work, with promising follicle-regeneration signals but minimal rigorous human data. This is a genuinely interesting research target, not a validated treatment. Mechanistically intriguing, clinically unproven.

Dosing: Reference (non-approved) only: used topically on the scalp in experimental and gray-market protocols, often with microneedling and sometimes alongside valproic acid; there is no established or approved dosing. Included strictly so you recognize it when a patient asks — not an endorsement, and not a protocol to replicate.

Monitoring: No standardized monitoring exists; treat any use as experimental, with attention to scalp irritation and the sourcing cautions that apply to all gray-market peptides.

Cautions: Unproven efficacy and unknown long-term safety in humans. A theoretical, general caution applies to any compound that activates regenerative growth pathways: such pathways intersect with cell proliferation, and the long-term implications in humans are unstudied. Gray-market sourcing risk is significant.

Counseling: "This is experimental — the science is interesting, but it hasn't been proven to work or shown to be safe in people, and it isn't approved. I can't recommend it as a treatment, and if you've encountered it online, the products are unregulated."

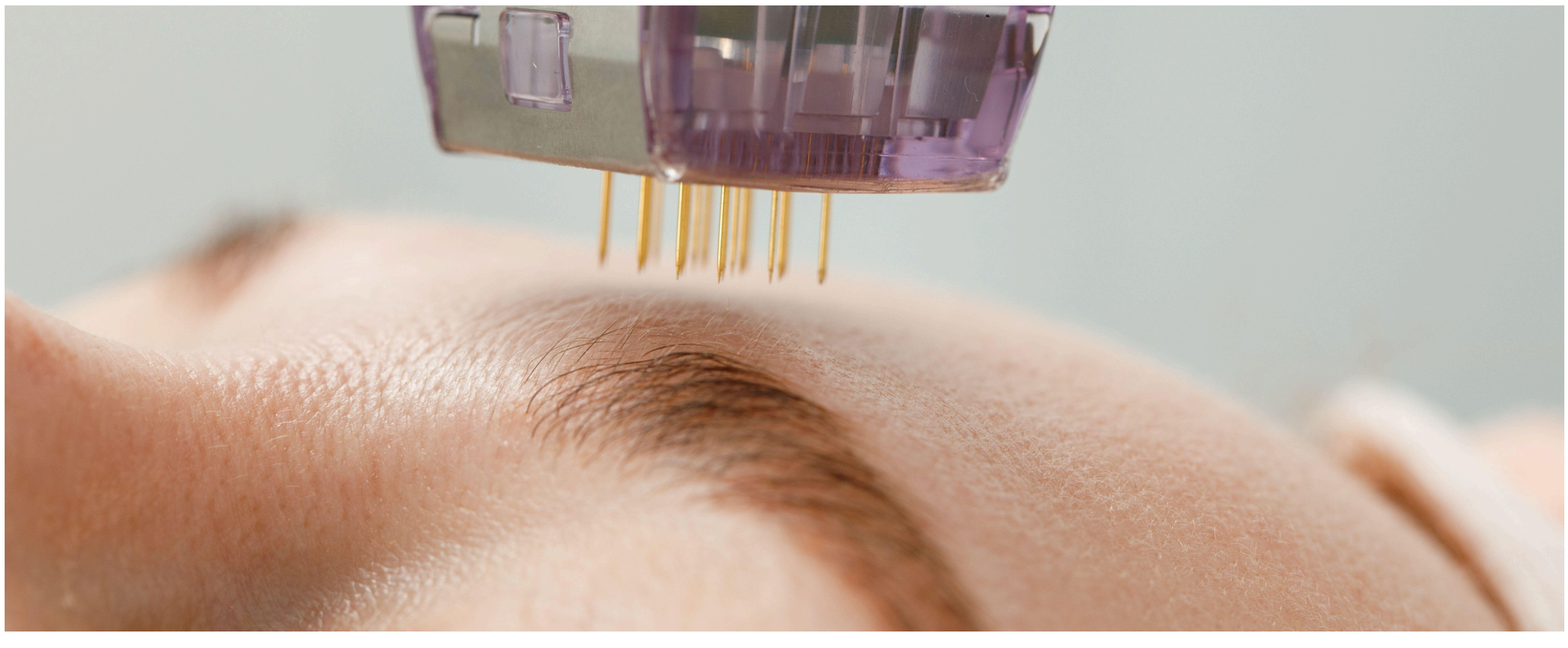


Procedural and Biologic Adjuncts (Brief)

Patients comparing peptides to other "regenerative" hair options will ask about these. They are not peptides, but a short, honest orientation prevents confusion.

Option	What It Is	Evidence	Honest Status
PRP (platelet-rich plasma)	Patient's own concentrated platelets injected into scalp	Moderate; several positive but heterogeneous studies	Reasonable adjunct; protocols vary widely
Exosomes	Cell-derived signaling vesicles applied/injected	Early, preliminary; heavily marketed	Investigational; regulatory status unsettled
Microneedling	Controlled micro-injury to stimulate repair and enhance topical penetration	Moderate, especially with minoxidil	Useful adjunct; often the delivery method for peptides

Table 7.2 — Biologic/Procedural Hair Adjuncts



Microneedling is worth a specific note: it is frequently the vehicle through which scalp peptides are delivered, and much of any observed benefit in "peptide + microneedling" protocols may come from the microneedling and the co-applied proven agents rather than the peptide itself — a confounder to keep in mind when judging results.

The Honest Verdict on Hair Peptides

Hair peptides occupy the plausible tier at best. GHK-Cu has a reasonable mechanistic rationale and a supportive-adjunct role; PTD-DBM is an intriguing research-stage target with no clinical validation. Neither belongs ahead of — or instead of — the proven standards. The defensible clinical posture is to anchor every hair-loss plan in evidence-based first-line therapy (minoxidil, finasteride where appropriate, and procedures with real data), and to position peptides explicitly as optional adjuncts with modest, unproven, or experimental support. As elsewhere, the practitioner's value is in honest framing: patients arriving with high hopes pinned on a peptide need to hear, kindly, where the evidence actually stands.



Key Takeaways:

- No peptide is a first-line or FDA-approved hair-loss treatment; peptides are adjuncts to proven standards (minoxidil, finasteride, procedures).
- GHK-Cu has a plausible mechanism and a supportive role, but hair-specific human evidence is weak and usually confounded by multi-ingredient products.
- PTD-DBM is an experimental Wnt-pathway peptide — mechanistically interesting, preclinical, unproven, with no established dosing; recognize it, don't recommend it.
- PRP, exosomes, and microneedling are non-peptide adjuncts patients ask about; microneedling is often the delivery vehicle and a major confounder when judging peptide results.
- Anchor hair plans in proven therapy and frame peptides honestly as optional, modest-evidence adjuncts.



8



RECOVERY AND WOUND-HEALING PEPTIDES

Overview

No corner of peptide therapy is marketed harder than "healing" and "recovery." BPC-157 and TB-500 are sold — usually together — as a near-magical injury-repair stack for tendons, ligaments, muscle, and gut.

The biology is genuinely interesting and the anecdotes are loud. The human evidence is thin, and the regulatory status is among the most precarious in this book. This chapter requires holding two ideas at once: the mechanisms are real and plausible, and the human outcome data is minimal. That tension — strong mechanism, strong marketing, weak human evidence, contested legality — defines the entire category.

Peptide	Marketed For	Human Evidence	Regulatory	WADA
BPC-157	Tendon, ligament, muscle, gut repair	Minimal (mostly animal)	Not approved; Category 2 / under review	Banned
TB-500	Soft-tissue and muscle repair	Minimal (mostly animal)	Not approved; Category 2 / under review	Banned
Thymosin β-4 (Tβ4)	The natural parent molecule	Some early human trials	Not approved (US)	Banned

Table 8.1 — The Recovery Peptides at a Glance

A recurring caution spans the whole chapter: these peptides are pro-angiogenic — they promote new blood-vessel growth. That is precisely how they're thought to aid healing, and it is also the basis of a genuine, unstudied theoretical cancer concern, since tumors depend on angiogenesis to grow. This shapes the cautions for every peptide here.

BPC-157 (Body Protection Compound-157)

Status: Not FDA-approved for any human indication. Designated FDA Category 2 / under advisory review (a "do not compound" safety flag). WADA-prohibited since 2022. One of the most legally precarious peptides in common use.

Mechanism: A synthetic peptide derived from a protective protein found in gastric juice. Proposed actions include promoting angiogenesis (new blood vessels to the injury site), modulating growth factors, exerting anti-inflammatory effects, and supporting the integrity of the gut lining. The mechanism is attractive and coherent — which is exactly why it is so heavily marketed.

Evidence: This is the crux. A 2025 systematic review screened 544 articles and included 36; 35 were preclinical (animal) and just one was human — a 12-patient, uncontrolled, unblinded knee-pain case series. In other words, there is essentially no high-quality human efficacy evidence, and reviewers cautioned against clinical use on that basis. The animal data is genuinely impressive, but rodents are not humans. One hopeful note: a randomized controlled trial for hamstring injury is now underway — the first of its kind — so real human data may finally be coming.

Dosing: Reference (non-approved), teaching only: commonly cited compounding/literature range is approximately 250–500 mcg subcutaneously, once or twice daily, sometimes near the injury site; oral forms are marketed for gut/GI claims. There is no established or approved protocol — these figures are included so you recognize what patients encounter, not as an endorsement.

Monitoring: No standardized monitoring exists. If a patient is using it, apply the sourcing/CoA discipline (Chapter 5), document the off-label/non-approved discussion, and screen for the cautions below.

Cautions: Long-term human safety data is absent. The central concern is the angiogenesis–cancer question: the same vessel-growth that may aid healing could theoretically support tumor growth, and this is unstudied in humans — so avoid in active or prior malignancy. WADA-banned: contraindicated for any tested athlete. Gray-market sourcing risk is high.

TB-500 / Thymosin β-4

Status: Not FDA-approved for any human indication. FDA Category 2 / under review. WADA-prohibited. Marketed as the constant companion to BPC-157.

A precision point — TB-500 ≠ Thymosin β-4: These are routinely treated as identical in marketing, but they are not the same molecule. Thymosin β-4 (Tβ4) is the natural, full-length protein, which has had some early human trials (in wound healing and cardiac contexts). TB-500 is a synthetic fragment marketed as its equivalent, with minimal direct human efficacy data. Stating this distinction is a mark of expertise and protects you from overstating the evidence.

Mechanism: Involved in actin regulation — helping cells migrate to sites of injury — along with promoting angiogenesis and reducing inflammation and fibrosis (scarring). The theory: cells reach and rebuild damaged tissue faster.

Evidence: Predominantly preclinical (animal and cell). The parent molecule, thymosin β-4, has limited early human data; TB-500 specifically has little direct human efficacy evidence, and there are no robust human RCTs for the soft-tissue claims it's sold for. Plausible mechanism, thin human proof.

Dosing: Reference (non-approved), teaching only: commonly cited range is approximately 2–2.5 mg subcutaneously, about twice weekly as a "loading" phase, then weekly maintenance. No established or approved protocol; included for recognition only.

Monitoring: No standardized monitoring. Same approach as BPC-157 — sourcing discipline, documentation, caution screening.

Cautions: Limited human safety data; long-term effects unknown. The same pro-angiogenic cancer caution applies — avoid in active or prior malignancy. WADA-banned for tested athletes. Gray-market sourcing risk.

Counseling: "There's interesting repair biology here, but it's mostly animal data — and note that TB-500 isn't the same as the thymosin β-4 that's actually been studied in humans. It's not FDA-approved and it's banned in sport."

Counseling: "The animal science is promising, but the human evidence is minimal, it's not FDA-approved, it's flagged by regulators, and it's banned in sport. I can't represent it as proven — and if you have any cancer history, it's off the table."

The BPC-157 + TB-500 Stack

These two are marketed as the injury-repair combination, with claims of synergy across complementary pathways (BPC-157's angiogenesis plus TB-500's cell migration). The honest reality: there are no controlled human trials of the combination. The synergy claim is theoretical, built by stacking two individually unproven compounds. Combining them also compounds the unknowns — additive side effects, unstudied interactions, harder attribution if something goes wrong, and, for athletes, two banned substances instead of one. More peptides multiply risk, not evidence.



The Cancer / Angiogenesis Caution in Depth

Because it governs the cautions for this whole chapter, it's worth stating plainly. Angiogenesis — the growth of new blood vessels — is a legitimate part of how tissue heals. It is also a hallmark of tumor progression: cancers must recruit a blood supply to grow beyond a tiny size, and pro-angiogenic signaling is one way they do it. BPC-157 and TB-500 are pro-angiogenic by design. Whether their use meaningfully affects cancer risk in humans is entirely unstudied — there is no evidence of harm, but also none of safety. The responsible posture in the face of that uncertainty is conservative: contraindicate in active or prior malignancy, take a careful personal and family cancer history, and disclose the theoretical concern in informed consent. This is mechanism plus biological plausibility, not proof — but it is not something to gamble with.

The Honest Verdict on Recovery Peptides

These peptides sit at the plausible end for mechanism and the hype end for proof. The biology is real enough to take seriously as a hypothesis; the human evidence is too thin to make confident clinical claims. Add a precarious regulatory status (Category 2 / under review), a blanket WADA ban, an unresolved cancer caution, and a gray-market supply chain, and the defensible clinical posture is clear: understand these peptides thoroughly, counsel patients on them honestly, and be very cautious about prescribing them — while watching for the human trial data that may, finally, be on the way. The practitioner's real value here is the honest conversation, not the prescription.



Key Takeaways:

- BPC-157 and TB-500 are marketed aggressively for injury/recovery; both have strong mechanisms but minimal human evidence, are not FDA-approved (Category 2/under review), and are WADA-banned.
- A 2025 systematic review found essentially no high-quality human efficacy data for BPC-157 (35 of 36 included studies were preclinical; the one human study was a 12-patient uncontrolled series); an RCT is now underway.
- TB-500 is not the same molecule as thymosin β-4 — the parent protein has some human data; the marketed fragment has little. Stating this distinction signals real expertise.
- The famous BPC-157 + TB-500 stack has no controlled human trials; combining them multiplies unknowns, not evidence.
- All are pro-angiogenic, creating a genuine but unstudied cancer caution — avoid in active or prior malignancy, take a cancer history, and disclose the concern.

9

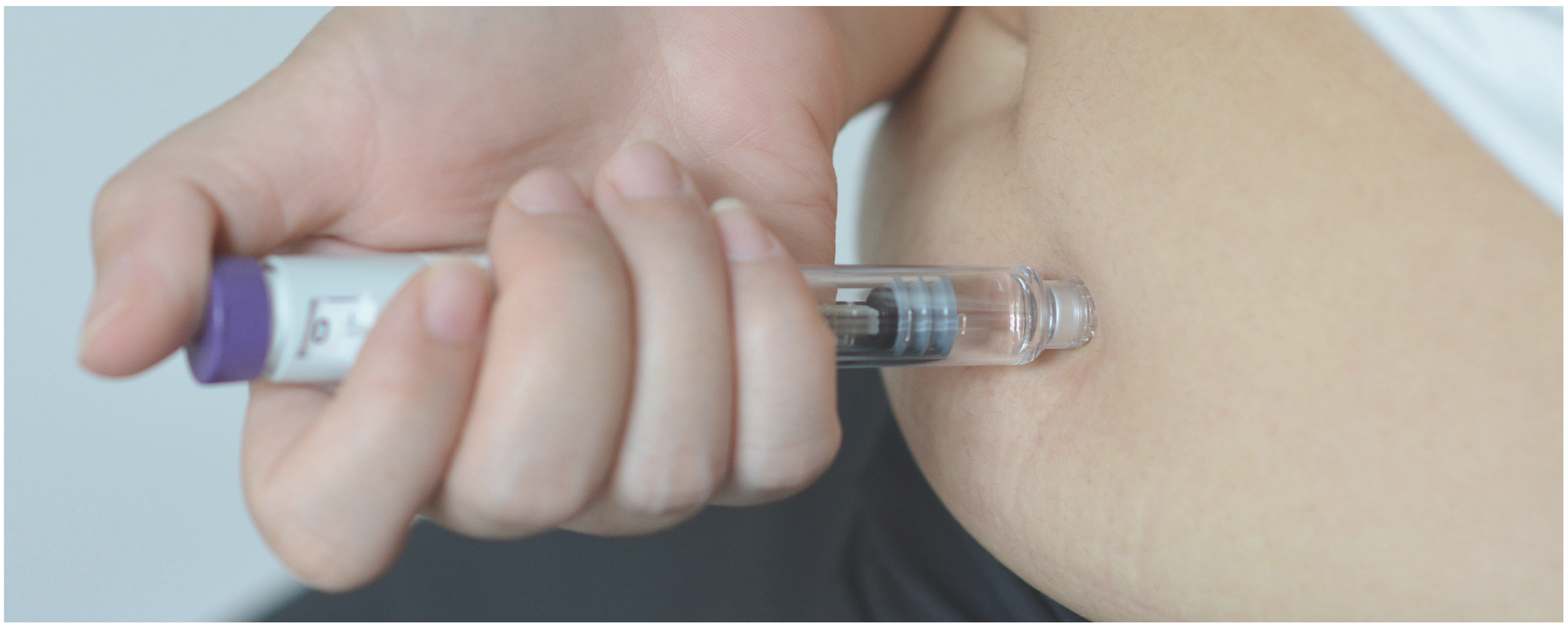


WEIGHT LOSS AND METABOLIC PEPTIDES

Overview

This is the chapter where peptide therapy is most evidence-based and most consequential. The incretin class — GLP-1 and GIP/GLP-1 agonists — represents the single biggest advance in obesity medicine in a generation, with FDA approval, large randomized trials, and weight-loss results that for decades were achievable only with surgery.

Because these are approved drugs, this chapter gives real, label-grade dosing you can prescribe from, within the appropriate indication.The chapter then steps down the evidence spectrum to the "beyond GLP-1" compounds — some plausible, some pure hype — and closes by flagging the aesthetic crossover (covered fully in Chapter 14), since rapid weight loss reshapes the face and body in ways that land directly in your chair.



Tier	Agents
Proven	Semaglutide, tirzepatide, liraglutide, dulaglutide (and the amylin analogs)
Plausible	Tesamorelin (metabolic/visceral fat — see Ch. 10), GH secretagogues (see Ch. 10), cagrilintide (in trials)
Hype	AOD-9604, MOTS-c, 5-Amino-1MQ

Table 9.1 — The Metabolic Peptides by Evidence Tier

How the Incretin Class Works

Two gut hormones — GLP-1 and GIP — are released when we eat and amplify insulin release, an effect called the incretin effect. GLP-1 has four relevant jobs: it stimulates insulin only when glucose is elevated (a built-in safety feature that keeps hypoglycemia risk low), suppresses glucagon, slows gastric emptying (the source of both prolonged fullness and the class's nausea), and acts centrally to reduce appetite and quiet "food noise." That central appetite effect — not metabolic speed-up — is the real engine of weight loss. Understanding these four jobs explains both the efficacy and the side-effect profile of every drug below.

Semaglutide

Status: FDA-approved. Ozempic/Rybelsus (type 2 diabetes), Wegovy (chronic weight management). Approved, well-characterized, with years of real-world data.

Mechanism: Selective GLP-1 receptor agonist. A fatty-acid chain binds albumin, extending half-life to ~1 week for once-weekly injection.

Evidence: Proven. In the STEP 1 trial (~1,961 adults, 68 weeks), semaglutide 2.4 mg produced ~14.9% mean weight loss vs. 2.4% placebo; 86% lost ≥5%, 69% ≥10%, 50% ≥15% (NEJM, 2021). It established the modern benchmark.

Dosing (label-grade):

Product	Route	Schedule
Wegovy (weight)	SC weekly	0.25 → 0.5 → 1.0 → 1.7 → 2.4 mg, escalating every 4 weeks
Ozempic (T2D)	SC weekly	0.25 (×4 wk) → 0.5 → 1.0 → up to 2.0 mg
Rybelsus (T2D, oral)	Oral daily	3 mg ×30 days → 7 mg → 14 mg; empty stomach, ≤4 oz water, wait 30 min

Table 9.2 semaglutide titration

Monitoring: Tolerability every 4 weeks during titration; response check ~16 weeks; weight, A1c (if diabetic), and side effects at maintenance (~every 3 months).

Cautions: **Boxed warning** — contraindicated with personal/family history of medullary thyroid carcinoma or MEN-2. Caution with pancreatitis history. Contraindicated in pregnancy; discontinue ~2 months before conception (long half-life). Reduce insulin/sulfonylureas to prevent hypoglycemia. Slowed gastric emptying raises aspiration risk under sedation (see Ch. 13–14).

Counseling: "This quiets appetite and 'food noise.' Expect gradual loss over months, some early nausea that usually settles, and understand it's chronic therapy — weight tends to return if you stop without a maintenance plan."

Tirzepatide

Status: FDA-approved. Mounjaro (type 2 diabetes), Zepbound (chronic weight management). The first approved dual agonist.

Mechanism: A single peptide acting at both GIP and GLP-1 receptors. The dual engagement is additive — possibly synergistic — producing greater weight loss than GLP-1 alone, and the GIP component may improve GI tolerability.

Evidence: Proven. In SURMOUNT-1 (~2,539 adults, 72 weeks), tirzepatide 15 mg produced ~20.9% mean weight loss vs. 3.1% placebo; 91% lost ≥5%, 57% lost ≥20% (NEJM, 2022) — approaching surgical outcomes.

Dosing (label-grade): SC weekly. 2.5 mg ×4 weeks (initiation, not therapeutic) → 5 mg, then increase by 2.5 mg at intervals of ≥4 weeks as needed. Maintenance: 5, 10, or 15 mg (max 15). Many patients stabilize at 5–10 mg — the goal is the lowest effective dose, not the maximum.

Monitoring: Same cadence as semaglutide.

Cautions: Same boxed warning (MTC/MEN-2) and the same pancreatitis, pregnancy, hypoglycemia, and sedation/aspiration cautions as the GLP-1 class.

Counseling: "This works on two receptors and tends to produce more weight loss on average than semaglutide — but it's the same family of side effects and the same long-term, chronic-therapy mindset."

Liraglutide

Status: FDA-approved. Saxenda (weight), Victoza (type 2 diabetes). The first GLP-1 approved for weight; now largely superseded by weekly agents but still in use.

Mechanism: GLP-1 receptor agonist with a shorter half-life requiring daily injection.
Evidence: Proven but more modest — typically ~5–8% weight loss, with a long safety record.

Dosing (label-grade): Saxenda (weight): SC daily, 0.6 → 1.2 → 1.8 → 2.4 → 3.0 mg in weekly steps. Built-in checkpoint: reassess at 16 weeks — discontinue if <4% body weight lost. Victoza (T2D): 0.6 mg ×1 week → 1.2 → max 1.8 mg.

Monitoring: As above; Saxenda's 16-week/4% rule is the one explicit labeled discontinuation threshold in the class.
Cautions: Same class cautions (boxed warning, pancreatitis, pregnancy, hypoglycemia, sedation).

Counseling: "It works, but it's a daily injection and the average results are more modest than the weekly drugs — and there's a clear 16-week check to see if it's working for you."

Agent	Brand	Use	Dosing (label-grade)	Note
Dulaglutide	Trulicity	T2D	SC weekly: 0.75 → 1.5 → 3.0 → 4.5 mg	Modest weight effect
Exenatide	Byetta / Bydureon	T2D	5→10 mcg BID; or 2 mg weekly	Older; largely superseded
Pramlintide	Symlin	Adjunct to insulin	Per label	FDA-approved amylin analog
Cagrilintide	(in CagriSema)	Investigational	Trial-stage	Long-acting amylin; with semaglutide

Table 9.3 — Additional Approved Incretin/Amylin Agents

The amylin pathway (pramlintide, cagrilintide) is a separate, proven satiety mechanism — co-secreted with insulin, it slows gastric emptying and reduces glucagon. CagriSema (semaglutide + cagrilintide) represents the dual-mechanism frontier in late-stage trials.

Beyond GLP-1: Plausible and Hype

Patients will bring "alternative" fat-loss peptides. Triaged honestly:

Peptide	Tier	The Honest Verdict
AOD-9604	Hype	hGH fragment marketed as "clean fat loss." An early 12-week RCT showed modest loss (2.6 vs 0.8 kg), but the larger 24-week pivotal trial failed; development terminated 2007. Not approved.
MOTS-c	Hype	Mitochondrial-derived "exercise mimic"; genuinely novel biology but almost entirely preclinical. "Exercise in a vial" is premature. Not approved.
5-Amino-1MQ	Hype	Not even a peptide — a small-molecule NNMT inhibitor. Preclinical only; no human RCTs. Calling it a "peptide" is a marketing red flag. Not approved.

Table 9.4 — "Beyond GLP-1" Agents

These are all teaching-only recognitions: no FDA approval, no established human-validated dosing, and no place ahead of proven therapy.



The Aesthetic Crossover (Preview)

These drugs don't just move the scale — they reshape the patient, which is why they belong in an aesthetics handbook. Rapid weight loss produces "Ozempic face" (volume loss, hollow temples, deflated cheeks, deeper folds), skin laxity outpacing the skin's ability to contract, and lean-muscle loss that affects body composition and support. These create new demand for volumizing, tightening, and muscle-preservation strategies — covered fully in Chapter 14.



Key Takeaways:

- The incretin class (GLP-1 and GIP/GLP-1 agonists) is the proven core of metabolic peptide therapy, with FDA approval and large RCTs; this chapter's dosing is label-grade and prescribable.
- Semaglutide (~15% loss, STEP 1) and tirzepatide (~21%, SURMOUNT-1) are the headline agents; liraglutide is older/daily/more modest with a labeled 16-week/4% checkpoint.
- The whole class shares a boxed warning (MTC/MEN-2) plus pancreatitis, pregnancy, hypoglycemia, and sedation/aspiration cautions — start low, go slow, monitor on a 4-week / 16-week / 3-month cadence.
- "Beyond GLP-1" agents (AOD-9604, MOTS-c, 5-Amino-1MQ) are hype-tier — unproven, unapproved, and not a substitute for proven therapy; note AOD-9604's failed pivotal trial and that 5-Amino-1MQ isn't even a peptide.
- Rapid weight loss drives an aesthetic crossover (facial volume loss, skin laxity, muscle loss) that is the practitioner's opportunity and responsibility — detailed in Chapter 14.

10



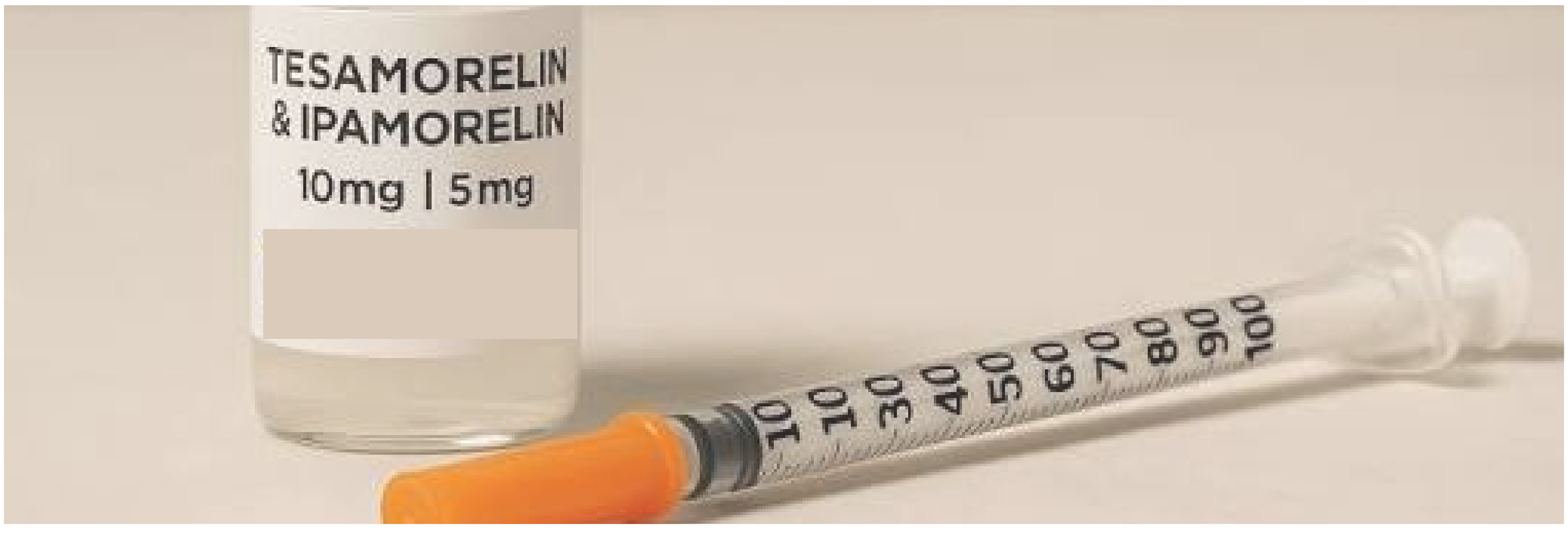
GROWTH HORMONE AXIS PEPTIDES

Overview

This class promises some of the most appealing outcomes in the field — fat loss, recovery, lean mass, "anti-aging" — and delivers some of the widest gap between biomarker and outcome. These peptides reliably raise growth hormone (GH) and IGF-1; what's far less established is whether moving those numbers produces the clinical results patients are sold.

One agent (tesamorelin) is genuinely FDA-approved for a narrow indication; the rest are non-approved, contested, and WADA-banned.

How the axis works: The hypothalamus releases GHRH, which tells the pituitary to release GH; GH acts on the liver to produce IGF-1, the downstream mediator of most GH effects. The body also makes ghrelin, which stimulates GH release through a separate receptor. The peptides in this class pull one of two levers:



Lever	Class	Examples	Effect
GHRH analogs	Mimic GHRH	Sermorelin, CJC-1295, tesamorelin	Stimulate pituitary GH release
Secretagogues / ghrelin mimetics	Mimic ghrelin (GHRP)	Ipamorelin, GHRP-2/6, MK-677	Amplify GH pulse via a second pathway

Table 10.1 — Two Levers on the GH Axis

A unifying caution governs the whole class: GH and IGF-1 are growth and anti-apoptotic signals — they tell cells to grow and not die. This is the basis of a real, unresolved cancer concern (detailed at the end of the chapter), and it shapes the cautions for every agent here. A second irony worth holding: in longevity science, lower IGF-1 signaling is associated with longer lifespan — so "more GH = younger" may point the wrong direction.

Tesamorelin

Status: FDA-approved (Egrifta) for HIV-associated lipodystrophy (excess visceral fat). The one genuinely approved, trial-backed agent in this chapter. Anything outside that indication is off-label.

Mechanism: A stabilized GHRH analog that stimulates physiologic pituitary GH release, raising GH and IGF-1.

Evidence: Proven for its indication — Phase III randomized trials show meaningful reduction in visceral adipose tissue in HIV lipodystrophy. Notably, it does not produce appetite suppression, and evidence outside its approved population is limited.

Dosing (label-grade): 2 mg subcutaneously once daily. Within the approved indication this is prescribable; any other use is off-label and must be justified and documented.

Monitoring: IGF-1 at baseline and periodically (keep age-appropriate, avoid supraphysiologic); fasting glucose/HbA1c (GH worsens insulin sensitivity); symptom review.

Cautions: Contraindicated in active malignancy and pregnancy. Can worsen glucose tolerance. The narrow indication means off-label use carries the usual documentation burden. Standard GH-axis cancer caution applies.

Counseling: "This is FDA-approved, but specifically for a particular type of visceral-fat problem. Used outside that, it's off-label — real drug, real data, but a narrow lane."

Sermorelin

Status: Not FDA-approved (the original branded product was withdrawn from the market for commercial reasons). Available compounded. Verify WADA status — secretagogues are banned for tested athletes.

Mechanism: A short GHRH analog (the active 1–29 fragment) that stimulates pituitary GH release. Being short-acting, it tends to preserve the natural nocturnal GH pulse rather than flatten it.

Evidence: Raises GH/IGF-1 (biomarker effect is real). Robust human outcome trials for body composition or anti-aging are lacking. Plausible mechanism, limited outcome data.

Dosing (reference, non-approved): Commonly cited around 0.2–0.3 mg subcutaneously at night (compounded). No established, approved protocol; included for recognition, not endorsement. Night dosing aligns with the natural GH surge.

Monitoring: IGF-1 (baseline + periodic, keep in age range), glucose/HbA1c, symptom review.

Cautions: Contraindicate active/prior malignancy; caution in diabetes/poor glycemic control. Gray-market/compounding quality risk. WADA-banned for tested athletes.

Counseling: "It nudges your own GH release and is gentler than synthetic GH, but the proof that it changes how you look or feel — rather than just your lab numbers — is thin, and it isn't FDA-approved."



CJC-1295 + Ipamorelin

Status: Not FDA-approved. FDA Category 2 / under review. WADA-banned. The most commonly compounded GH-axis combination in practice.

Mechanism: CJC-1295 is a long-acting GHRH analog; ipamorelin is a selective ghrelin-mimetic secretagogue (valued for raising GH without strongly triggering cortisol or prolactin). Together they amplify the GH pulse through two pathways. A formulation note: CJC-1295 with DAC is long-acting and flattens the pulse into sustained elevation; without DAC (mod GRF 1-29) is short-acting and preserves pulsatility — a meaningful difference in effect.

Evidence: The combination reliably raises GH/IGF-1 (well-documented biomarker effect), but there are no robust human outcome trials for the weight-loss, body-composition, or anti-aging claims it's sold for. The textbook biomarker-vs-outcome gap.

Dosing (reference, non-approved): Commonly cited around 100 mcg of each, subcutaneously, at night (short-acting forms), often together.

No established or approved protocol; for recognition only.

Monitoring: IGF-1 (baseline + periodic; the anchor lab and the cancer-risk guardrail — if it climbs above age range, reduce or stop), glucose/HbA1c, prolactin (with GHRPs), and symptom review.

Cautions: Contraindicate active/prior malignancy. CJC-1295 carries some cardiac and immunogenicity concerns; FDA review of GH-axis compounds has noted serious adverse events, including reports of death across several of these peptides. WADA-banned. Gray-market risk.

Counseling: "This combo reliably raises your growth-hormone numbers — but that's a lab change, not a proven result. It isn't FDA-approved, it's flagged by regulators, it's banned in sport, and we'd monitor your IGF-1 closely if you used it."

MK-677 (Ibutamoren)

Status: Not FDA-approved. Not a peptide — an orally active small-molecule ghrelin-receptor agonist. WADA-banned.

Mechanism: A sustained oral secretagogue that raises GH and IGF-1 continuously — which flattens the natural pulse rather than mimicking it.

Evidence: Reliably raises GH/IGF-1; convenient because oral. Human outcome evidence for the marketed benefits is limited, and the sustained elevation profile raises particular concern.

Dosing (reference, non-approved): Commonly cited around 10–25 mg orally once daily. No established or approved protocol; for recognition only.

Monitoring: IGF-1, and especially fasting glucose/HbA1c — MK-677 is the worst of this group for insulin resistance. Watch for edema and appetite increase.

Cautions: Notable for water retention, increased appetite, and worsening insulin resistance/blood sugar. Contraindicate active/prior malignancy. The continuous, non-pulsatile elevation is theoretically less physiologic. WADA-banned; gray-market risk.

Counseling: "It's a convenient oral option, but it's not a peptide and not FDA-approved, it can raise your blood sugar and cause water retention and hunger, and it's banned in sport."



The Cancer Question (GH Axis)

This caution governs the entire class and deserves explicit statement. IGF-1 is a growth-promoting, anti-apoptotic signal — it drives cells to proliferate and resist programmed death, which is exactly the behavior cancer exploits. The epidemiology aligns: higher IGF-1 levels are associated with prostate, breast, and colorectal cancer, and the acromegaly model (chronic GH excess) shows organ enlargement, cardiovascular strain, and shortened lifespan. This is mechanism plus association, not proof of causation in the context of therapeutic peptide use — but it is not something to gamble with. The rules that follow:

- Contraindicate in active or prior malignancy.
- Screen with age-appropriate cancer screening before and during use.
- Anchor to IGF-1: keep levels age-appropriate, never supraphysiologic; rising IGF-1 means reduce the dose or stop.
- Disclose the concern explicitly in informed consent.

The Honest Verdict on GH-Axis Peptides

Tesamorelin aside, this class is proven to raise hormones and not proven to deliver the promise. The agents reliably move IGF-1 — a biomarker — while the outcomes patients actually want (fat loss, anti-aging, recovery) rest largely on mechanism and marketing rather than human trials. Layer on real side-effect burdens (insulin resistance, fluid retention, joint symptoms), a contested regulatory status, a blanket WADA ban, and an unresolved cancer concern, and the defensible posture is conservative: prescribe tesamorelin within its lane, treat the rest as non-approved options requiring honest counseling and tight IGF-1-anchored monitoring, and be the clinician who declines as readily as prescribes. "More GH" is not self-evidently good — and may, on the longevity evidence, be the wrong goal entirely.

Key Takeaways:

- The GH axis runs GHRH → GH → IGF-1, with two drug levers: GHRH analogs (sermorelin, CJC-1295, tesamorelin) and ghrelin-mimetic

Key Takeaways:

secretagogues (ipamorelin, GHRP-2/6, MK-677).

- Tesamorelin is the one FDA-approved agent (HIV visceral fat, 2 mg SC daily); everything else is non-approved, mostly Category 2/contested, and WADA-banned.
- The class reliably raises GH/IGF-1 (a biomarker) but lacks robust human outcome trials for its marketed benefits — the central biomarker-vs-outcome gap.
- MK-677 is a small molecule, not a peptide, and is the worst of the group for insulin resistance and fluid retention; CJC-1295 "with vs. without DAC" determines pulsatile vs. sustained signaling.
- A real, unresolved cancer concern (IGF-1 is pro-growth and anti-apoptotic; higher IGF-1 associates with several cancers) demands: contraindicate in malignancy, screen, anchor monitoring to IGF-1, and disclose in consent.

11



SEXUAL HEALTH, COGNITION, AND LONGEVITY PEPTIDES

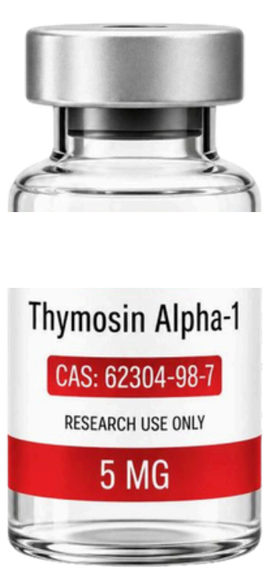
Overview

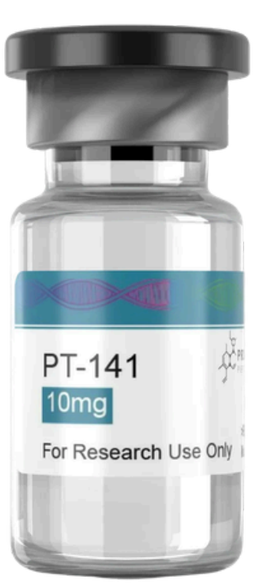
This chapter covers the peptides patients are often most curious — and most secretive — about: libido, focus, mood, immunity, and "anti-aging." It also spans the widest evidence range in the book, from a genuinely FDA-approved drug (PT-141) to compounds whose entire appeal is telomere-lengthening marketing (epitalon). That range makes it the ideal final exercise in the triage skill from Chapter 3: same chapter, opposite ends of the spectrum.

Domain	Peptide	Tier	Status
Sexual health	PT-141 (bremelanotide)	Proven (its indication)	FDA-approved (Vyleesi)
Cognition/mood	Semax	Plausible	Approved in Russia; not FDA/EMA
Cognition/mood	Selank	Plausible	Approved in Russia; not FDA/EMA
Immune	Thymosin α-1	Plausible–proven (abroad)	Approved in ~30+ countries; not US
Longevity	Epitalon	Hype	Not approved anywhere

Table 11.1 — This Chapter's Peptides by Domain and Tier







PT-141 (Bremelanotide)

Status: FDA-approved (Vyleesi) for acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women. Use outside that population is off-label. One of the few approved peptides in this chapter.

Mechanism: A melanocortin receptor agonist (same family as the Melanotan skin peptides). Crucially, it acts on the brain's desire pathways, not on blood flow — making it mechanistically distinct from PDE5 inhibitors like sildenafil. The shorthand: Viagra is plumbing, PT-141 is wiring.

Evidence: Proven for its indication. Approval rested on randomized, placebo-controlled trials (RECONNECT) showing a modest but real improvement in sexual desire and a reduction in associated distress. The effect is meaningful for some, not dramatic for all — set expectations accordingly.

Dosing (label-grade): 1.75 mg subcutaneously, as needed, roughly 45 minutes before anticipated activity. Maximum one dose per 24 hours and eight per month.

Monitoring: Blood pressure awareness (transient rise after dosing); tolerability, especially nausea; pigmentation with repeated use.

Cautions: Causes a transient rise in blood pressure after each dose — avoid in uncontrolled hypertension or known cardiovascular disease. Nausea is common and can be significant, limiting adherence. Repeated use can cause focal hyperpigmentation (a melanocortin-family effect). Contraindicated in pregnancy. Off-label use (e.g., in men) is widespread but outside the label — counsel and document.

Counseling: "It works on desire in the brain, it's FDA-approved for a specific group, expect some nausea, and it briefly raises blood pressure. Approved doesn't mean risk-free."

Semax

Status: Not FDA- or EMA-approved. Approved and prescribed in Russia for decades (e.g., stroke, cognitive indications). A real but limited, largely non-Western evidence base.

Mechanism: A synthetic peptide derived from a fragment of ACTH, marketed as a nootropic. Proposed actions: increasing BDNF (brain-derived neurotrophic factor, supporting neuronal plasticity) and modulating dopamine and serotonin systems.

Evidence: Most human data is Russian, older, and not to modern Western RCT standards, supplemented by animal work. Promising signals, but not the evidence base of an approved Western drug. The credibility nuance: "approved in one country" is not the same as "validated by rigorous RCTs."

Dosing (reference, non-approved): Typically intranasal drops; cited daily ranges vary widely. No FDA-approved dose; included for recognition, not endorsement.

Monitoring: No standardized monitoring; watch for interactions with psychiatric medications.

Cautions: Generally reported as well-tolerated short-term; long-term and large-scale safety data are limited. Unknown interactions with psychiatric drugs warrant caution. Verify WADA status for tested athletes. Gray-market sourcing risk.

Counseling: "It's a real drug in Russia with limited Western evidence, it's not FDA-approved, and it shouldn't replace proper evaluation if you're dealing with genuine cognitive or mood concerns."

Selank

Status: Not FDA- or EMA-approved. Approved in Russia as an anxiolytic. Same evidence caveats as semax.

Mechanism: A synthetic peptide based on the natural immunomodulatory peptide tuftsin, marketed for anxiety and calm. Proposed to influence GABA and serotonin signaling and to modulate BDNF and immune pathways.

Evidence: Mostly Russian human studies plus animal data; few large, blinded, modern Western RCTs. Plausible anxiolytic signal, not Western-validated.

Dosing (reference, non-approved): Typically intranasal, daily dosing in cited protocols. No FDA-approved dose; for recognition only.
Monitoring: No standardized monitoring; caution alongside psychiatric medication.

Cautions: Reported as well-tolerated short-term; limited long-term data. The key clinical caution is substitution — patients reaching for

Thymosin α-1

Status: Not FDA-approved (US). Approved in ~30+ countries (brand Zadaxin), with genuine clinical-trial history. In the US it is off-label/compounded. The strongest evidence base of the back-half peptides.

Mechanism: A naturally occurring thymic peptide that acts as an immune modulator — tuning immune responses toward balance rather than simply stimulating or suppressing.

Evidence: Real human clinical trials exist — used internationally as an adjunct in hepatitis B/C and certain cancers, and studied during COVID-19 for immune regulation. Stronger than most peptides in this part of the book, though still not FDA-approved domestically.

Dosing (reference, non-approved in US): Commonly cited around 1.6 mg subcutaneously, 1–2× weekly for wellness/immune use; approved-country protocols differ by indication. Verify against current status.

Monitoring: Clinical response and tolerability; immune-relevant history.

Cautions: Generally well-tolerated in trials. Caution in autoimmune disease and in immunosuppressed or transplant patients — modulating immunity cuts both ways. US off-label/compounding status applies.

Counseling: "This one actually has real clinical use abroad as an immune modulator, but it's not FDA-approved here, so it's off-label — and we'd be cautious if you have any autoimmune condition."



Epitalon

Status: Not approved anywhere. Evidence is almost entirely preclinical plus small older Russian studies. Sold on bold anti-aging marketing.

Mechanism: A synthetic peptide based on epithalamin (a pineal-gland extract), marketed with the strongest longevity language in the field: claimed to activate telomerase, lengthen telomeres, and slow aging.

Evidence: Almost entirely preclinical, with small, older human studies and no robust modern human RCTs. The telomere/lifespan-extension claims are unproven in people. Hype tier.

Dosing (reference, non-approved): Cited in cycles, e.g., ~5–10 mg/day subcutaneously for short courses, periodically. No established protocol; not approved anywhere; for recognition only.

Monitoring: No standardized monitoring exists.

Cautions: The central concern is the telomere–cancer paradox: telomerase activation is exactly what many cancers exploit to become "immortal." Promoting telomerase as "anti-aging" carries a real, unstudied cancer implication. Unknown long-term safety; gray-market risk.

Counseling: "The anti-aging claims are exciting, but human evidence is essentially absent, it isn't approved anywhere, and the very mechanism it's sold on — switching on telomerase — has real, unstudied cancer implications. I can't recommend it."

The Honest Verdict

This chapter is the triage skill in one page. Thymosin α-1 earns genuine credit — real trials, approved across many countries — while sitting off-label in the US. PT-141 is a true FDA-approved drug within a defined indication. Semax and selank are real foreign pharmaceuticals with thin Western evidence — interesting to discuss, never a substitute for proper psychiatric care. Epitalon is longevity hype with a serious, unstudied cancer caution. Same module, opposite ends of the spectrum — and the lesson is that the category ("sexual health," "cognition," "longevity") tells you nothing about the evidence. Triage every peptide individually, on its own human data.

Key Takeaways:

- This chapter spans the full evidence spectrum — from FDA-approved (PT-141) to pure hype (epitalon) — making category labels useless and individual triage essential.
- PT-141 is FDA-approved for premenopausal HSDD (1.75 mg SC PRN, ~45 min before, max 1/24h & 8/month); it acts on brain desire pathways, raises BP transiently, and commonly causes nausea.
- Semax and selank are approved in Russia with limited Western evidence; their key caution is not replacing proper evaluation of real cognitive or anxiety concerns.
- Thymosin α-1 has the strongest evidence here — approved in ~30+ countries as an immune modulator — but is off-label in the US; use caution in autoimmune/immunosuppressed patients.
- Epitalon is unapproved longevity hype; its telomerase-activation pitch carries a genuine, unstudied cancer implication — recognize it, don't recommend it..



Part III
Clinical Practice

12



PATIENT SELECTION, CONSULTATION, AND INFORMED CONSENT

Anyone Can Prescribe; Prescribing Well Is the Skill

The difference between a good outcome and a harmful one rarely lies in the molecule. It lies in who you selected, how you consulted, and what you documented. Most peptide harm — and most liability — traces back to a rushed or skipped consultation.

A structured workflow is therefore both your best clinical tool and your best legal protection.

The Consultation Workflow

Run the same six steps, in the same order, for every patient.

Step	Action	Key Question
1. Intake & goals	Establish what they want and why now	Is this a realistic clinical goal or a marketing-driven wish?
2. History & screening	Full medical, medication, family history + class-specific screens	What in their history changes candidacy?
3. Candidacy decision	Green / yellow / red triage	Approved, justifiable off-label, or untenable?
4. Education & expectations	Explain mechanism, realistic results, timeline, risks	Do they understand what this will and won't do?
5. Informed consent	Peptide-specific written consent	Is the off-label/non-approved status explicit?
6. Baseline & plan	Labs, titration schedule, follow-up, instructions	Is the whole plan set before they leave?

Table 12.1 — The Six-Step Consultation Workflow

Step 1 — Intake and Goals

Distinguish a realistic clinical goal from a marketing-driven wish. A patient who says "I want to lose weight and keep it off" is different from one who says "I saw BPC-157 online and want to try it." The first describes a problem; the second names a product.

Reframe product-seeking back toward the underlying goal, then match the goal to the evidence.

Step 2 — History and Class-Specific Screening

A full history is the baseline. On top of it, each peptide class carries a specific screen that must not be skipped:

If considering...	Screen specifically for...
GLP-1 / metabolic	Personal/family medullary thyroid carcinoma or MEN-2 (boxed warning); pancreatitis; eating disorder history
GH-axis	Active or prior malignancy; diabetes/glycemic control
BPC-157 / TB-500	Active or prior malignancy; athletic drug-testing status
Any recovery/performance peptide	Drug-testing status (sport, military, employer)
Sexual-health (PT-141)	Uncontrolled hypertension, cardiovascular disease

Table 12.2 — Class-Specific Screening

This single table operationalizes the cautions scattered through Part II into one screening reflex.

Step 3 — The Candidacy Decision

A fast, defensible triage:

- Green — approved drug, clear indication, no contraindications. Proceed.
- Yellow — off-label but clinically justifiable. Proceed only with explicit reasoning documented.
- Red — contraindicated, unrealistic, or legally untenable. Decline or refer.

Saying no is part of the job. Not every patient is a candidate, and declining protects both of you. Always offer the safer alternative rather than a bare refusal — it preserves trust and steers the patient toward something legitimate.

Step 4 — Education and Expectations

Explain mechanism, realistic results, timeline, and side effects in plain language. State the regulatory status out loud — approved, off-label, or non-approved — because patients are entitled to know which they're choosing. Under-promise; the fastest route to a disengaged, dissatisfied patient is inflated expectations.

Step 5 — Informed Consent

Consent for peptide therapy should be written and peptide-specific, and must capture: the drug and dose, its FDA/regulatory status (explicitly including off-label or non-approved use), the realistic benefits, the known and unknown risks, the available alternatives, and — where relevant — the cancer and anti-doping cautions. Document the patient's questions and your answers. Re-consent whenever the protocol changes. Generic clinic consent forms are inadequate here; the non-approved status of many peptides makes specific, documented consent essential.

Step 6 — Baseline and Plan

Order baseline labs appropriate to the peptide (see Chapter 13), set the titration and follow-up schedule before the patient leaves, and provide written instructions plus clear "how to reach us / when to seek emergency care" guidance.

Red Flags in the Consultation

Trust the pattern when you see it: doctor-shopping for a specific banned or contested peptide, unrealistic expectations, minimizing

of risks, or pressure to "just prescribe." Any of these is a signal to slow down or decline.

Key Takeaways:

- Most peptide harm traces to a rushed consult; a fixed six-step workflow is your core clinical and legal safeguard.
- Layer a class-specific screen onto every full history (MTC/MEN-2 for GLP-1, malignancy for GH-axis/BPC, testing status for athletes, BP for PT-141).
- Triage candidacy green/yellow/red, and treat "no" as a legitimate, trust-building outcome.
- Consent must be written, peptide-specific, and explicit about non-approved status, cancer, and anti-doping cautions; re-consent on any change.
- Set labs, titration, and follow-up before the patient leaves, and trust consultation red flags.

13



TITRATION, MONITORING, AND MANAGING ADVERSE EVENTS

Start Low, Go Slow

Escalating too fast is the single most common cause of unnecessary side effects and early discontinuation. Patience in titration is clinical skill, not timidity. The goal is always the lowest effective dose, not the highest tolerated one — and the titration ladder bends to the patient, not the other way around.

The Monitoring Cadence

Across peptide classes, a consistent rhythm applies, adapted to the specific agent's labeled checkpoints:

Phase	Timing	Focus
During titration	Every ~4 weeks	Tolerability before each dose increase; adherence; technique
Response check	~16 weeks / 3–4 months	Is it working? (e.g., GLP-1 ≥5%; Saxenda's <4% stop rule)
Maintenance	Every ~3 months	Weight/effect, labs, side effects, long-term strategy

Table 13.1 — General Monitoring Cadence

The art of titration: hold the dose when a patient struggles (persistent nausea or GI distress means stay put — comfort drives compliance), recognize there is no prize for rushing to the maximum dose, and document every decision — why you held, why you escalated, what the patient reported. That record is both good care and your protection.



Baseline and Ongoing Labs

Tailor to the peptide, but a general framework:

Class	Baseline	Ongoing
GLP-1 / metabolic	Weight/BMI, metabolic panel, HbA1c, lipids, pregnancy test, med review	Weight, HbA1c (if diabetic), tolerability
GH-axis	IGF-1, fasting glucose/HbA1c, malignancy screen	IGF-1 (keep age-appropriate), glucose, prolactin (with GHRPs)
Recovery (BPC/TB)	Cancer history; no standardized labs	Clinical; sourcing discipline
PT-141	Blood pressure, CV history	BP awareness, pigmentation

Table 13.2 — Baseline and Monitoring Labs by Class

For metabolic patients on insulin or sulfonylureas, reduce those agents proactively at baseline to prevent hypoglycemia.



Recognizing and Managing Adverse Events

Most side effects are mild and manageable; a few demand urgent action. Teach patients which is which.

Sign	Concern	Action
Severe, persistent epigastric pain	Pancreatitis	Hold drug; check lipase/amylase; evaluate now
Right-upper-quadrant pain + nausea	Gallstones/cholecystitis (GLP-1 raises risk)	Urgent biliary workup
Persistent vomiting + reduced intake	Volume depletion / acute kidney injury	Hold; monitor renal function
Hypoglycemia	Especially with insulin/sulfonylureas	Treat; reassess concurrent agents
Hives, facial/lip swelling, wheeze	Allergic reaction / anaphylaxis	Emergency response; epinephrine; EMS

Table 13.3 — Red Flags Requiring Urgent Evaluation

The aesthetic-practice aspiration alert (critical for any clinic doing sedation): GLP-1 agents significantly delay gastric emptying, so the stomach may not be empty even after standard fasting. In patients undergoing sedation or general anesthesia, this is a real aspiration risk. Hold GLP-1 therapy before any sedated procedure, follow current ASRA/ASA guidance on hold periods, inform the anesthesia team, and document the hold. If your practice performs sedation, make this a standing policy.



The Long Game

Peptide therapy — especially metabolic therapy — is a tool, not a cure. Protect lean mass (significant weight loss includes muscle, so prescribe protein and resistance training as part of the plan, not optional add-ons), frame therapy as chronic where the condition is chronic, and set the expectation early that weight returns if therapy stops without lifestyle infrastructure in place.

The Cancer Question: IGF-1, Angiogenesis, and When to Say No

Two distinct mechanisms in this book intersect with cancer biology, and both warrant a conservative posture. They are not proof of harm — but they are not things to gamble with.

The IGF-1 pathway (GH-axis peptides). IGF-1 is a growth-promoting, anti-apoptotic signal — it drives cells to proliferate and resist programmed death, precisely the behavior cancer exploits. Higher IGF-1 levels are epidemiologically associated with prostate, breast, and colorectal cancer, and the acromegaly model (chronic GH excess) shows organ enlargement and shortened lifespan. This is mechanism plus association, not established causation from therapeutic peptide use — but the implication is clear.

The angiogenesis pathway (recovery peptides). BPC-157 and TB-500 are pro-angiogenic by design — they grow new blood vessels to aid healing. Tumors also depend on angiogenesis to grow beyond a minimal size. Whether these peptides meaningfully affect human cancer risk is entirely unstudied: no evidence of harm, but none of safety.

A third flag (longevity). Epitalon's selling point — telomerase activation — is the very mechanism many cancers use to become immortal, an unstudied implication packaged as anti-aging.

The unifying rules — when to say no:

- Contraindicate any of these peptides in patients with active or prior malignancy.
- Take a thorough personal and family cancer history, and conduct age-appropriate cancer screening.
- For GH-axis agents, anchor monitoring to IGF-1: keep it age-appropriate, never supraphysiologic; rising IGF-1 means reduce the dose or stop.
- Disclose the relevant concern explicitly in informed consent.
- When uncertainty is high and the indication is cosmetic or unproven, the right answer is often simply no.

This is the section to return to whenever a patient's enthusiasm outruns the evidence. The willingness to decline is what separates a defensible practice from a reckless one.

Key Takeaways:

- Start low and go slow to the lowest effective dose; monitor on a 4-week / 16-week / 3-month cadence and document every titration decision.
- Tailor baseline and ongoing labs by class; anchor GH-axis monitoring to IGF-1, and reduce insulin/sulfonylureas proactively in metabolic patients.
- Know the urgent red flags (pancreatitis, gallstones, AKI from volume loss, hypoglycemia, anaphylaxis) and teach patients to recognize them.
- The GLP-1 aspiration risk under sedation is a critical, clinic-specific safety issue — hold before sedated procedures and make it policy.
- The cancer question (IGF-1, angiogenesis, telomerase) demands a conservative posture: contraindicate in malignancy, screen, anchor to IGF-1, disclose, and be ready to say no.

14



THE AESTHETIC CROSSOVER AND COMBINATION PROTOCOLS

Why Metabolic Medicine Became Aesthetic Medicine

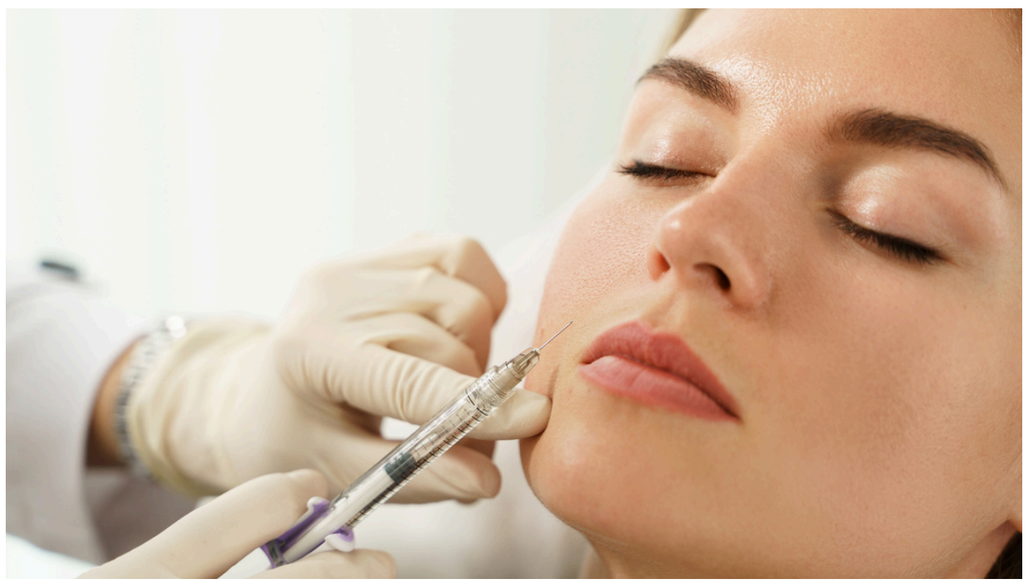
The GLP-1 revolution didn't just change the scale — it changed the face and body, and in doing so it landed squarely in aesthetic practice. Patients who lose 15–20% of their body weight rapidly look different in ways that create new clinical demand. Understanding this crossover is now a core competency, not a niche interest.

The Three Crossover Challenges

Challenge	What Happens	Aesthetic Response
"Ozempic face"	Facial fat loss → hollow temples, deflated cheeks, deeper folds; older-looking face on a younger-looking body	Volumizing (fillers, biostimulators), fat-preservation counseling
Skin laxity	Weight loss outpaces skin's ability to contract — face, neck, arms, abdomen, thighs	Skin-tightening procedures, energy-based devices, realistic staging
Lean-muscle loss	Total-mass loss includes muscle, reducing structural support and quality of result	Protein + resistance training; muscle-preservation as part of the plan

Table 14.1 — Aesthetic Consequences of Rapid Weight Loss

The clinical insight: a patient can be thrilled with their weight and unhappy with their face — and the second problem is the one that walks into your aesthetics chair. Anticipating it lets you counsel proactively rather than react after the change.



Principles of Combination Protocols

Patients and marketing both push toward "stacking" — combining peptides for compounding effect. The honest principles:

- Stacking multiplies unknowns, not evidence. The famous combinations (BPC-157 + TB-500; CJC-1295 + ipamorelin) have no controlled human trials of the combination. Each added agent adds side-effect potential, interaction risk, harder attribution, and — for athletes — another banned substance.
- Combine proven with proven cautiously, unproven with nothing. Layering an approved metabolic agent with established aesthetic procedures (fillers, energy devices, good skincare) is reasonable. Layering multiple non-approved peptides is where risk compounds without evidence.
- Sequence intelligently. For the weight-loss patient, the rational sequence is: achieve and stabilize weight first, preserve muscle throughout, then address residual facial volume and skin laxity once the weight is stable — chasing a moving target wastes filler and money.



The Defensible Crossover Plan

A reasonable, evidence-anchored approach to the GLP-1 aesthetic patient: prescribe or coordinate the metabolic therapy within its approved use; build in muscle preservation (protein, resistance training) from day one; monitor facial and skin changes over the weight-loss course; and time volumizing and tightening interventions to stabilized weight. This positions peptides and procedures as complementary tools within one coherent plan — not a pile of stacked compounds.

Key Takeaways:

- Rapid GLP-1 weight loss reshapes the face and body, creating three predictable challenges: "Ozempic face," skin laxity, and lean-muscle loss.
- The crossover is now core aesthetic practice — patients happy with their weight often arrive unhappy with their face.
- Stacking peptides multiplies unknowns, not evidence; the popular combinations have no controlled human trials.
- Combine proven-with-proven cautiously and sequence interventions to stabilized weight; build muscle preservation in from the start.

15



RUNNING A COMPLIANT, DEFENSIBLE PRACTICE

A Program, Not a Product

Anyone can sell a vial; building a peptide program means systems, compliance, and durability. Four pillars hold it up — clinical infrastructure, compliant marketing, sound pricing, and risk management — and a weakness in any one threatens the whole.

Pillar 1 — Clinical Infrastructure

Standardize the consultation workflow (Chapter 12) and maintain written protocols for each peptide. Build vetted relationships with licensed 503A/503B pharmacies, keep a Certificate of Analysis on file for every batch, establish a lab partner and a follow-up/recall system, and have an emergency protocol posted. Build your formulary deliberately: lead with FDA-approved agents, decide consciously whether to offer any contested/non-approved peptides (and document why), and re-verify regulatory status on a set schedule.

Pillar 2 — Compliant Marketing

This is the highest-liability area in the whole practice.



Do	Don't
Make truthful, substantiated claims	Use "miracle," "cure," "reverses aging," "guaranteed"
Disclose off-label/non-approved status	Call a compounded peptide "identical" to the brand drug
Substantiate before/after representations	Imply atypical results are typical
Govern claims made on your behalf	Let influencers make unsubstantiated claims unchecked

Table 15.1 — Marketing Do's and Don'ts

The "never say identical" rule is specific and enforced — the FDA has issued warning letters for exactly this. Compounded products are not FDA-approved equivalents, and representing them as such to patients or payers is a direct liability. You are also responsible for claims made on your behalf on social media.

Pillar 3 — Telehealth and Pricing

Telehealth: A valid practitioner-patient relationship is required; you must be licensed in the patient's state and honor that state's telehealth rules. Asynchronous, questionnaire-only prescribing is a high-risk model widespread in the GLP-1 space — know your state's stance before relying on it.

Pricing ethics: Be transparent and separate the medical fee from the product cost. Don't let margin drive the prescription — charge fee-for-service on the clinical care, not commission on the drug, and avoid incentives that reward over-prescribing. Patients can sense the difference, and so can regulators.

Pillar 4 — Risk Management

Carry malpractice coverage that explicitly includes peptide/aesthetic therapy — verify it in writing rather than assuming. Document everything (consent, candidacy reasoning, follow-up), maintain an adverse-event reporting pathway, and define clear discontinuation criteria. Practice within your license and training, and refer beyond it.

Staying Current Is a System

Because regulatory status is a snapshot, build a process to catch changes: assign someone to monitor FDA / Category 2 / WADA updates, schedule protocol reviews, and update consents when rules shift. The list changes — your process is what catches it.

The Compliance Scorecard

Pillar	Check
Formulary	Approved-first; non-approved offerings documented
Marketing	Substantiated; no "identical," no miracle claims
Telehealth	Valid relationship; correct-state licensure
Pricing	Transparent; care-based, not commission-based
Documentation	Consent, candidacy, follow-up all recorded
Insurance	Coverage confirmed in writing for peptide/aesthetic use

Table 15.2 — Six-Point Self-Audit

If you can't check all six, fix it before you scale.

Key Takeaways:

- A durable peptide program rests on four pillars: clinical infrastructure, compliant marketing, sound pricing, and risk management.
- Marketing is the highest-liability area — make substantiated claims, disclose status, and never call a compounded

peptide "identical" (the FDA issues warning letters for this).

- Telehealth requires a valid relationship and correct-state licensure; questionnaire-only prescribing is high-risk.
- Price ethically — fee-for-service on care, not commission on product — and carry malpractice coverage you've verified covers peptides.
- Treat staying current as a built-in system, and run the six-point compliance scorecard before scaling.

Back Matter

Master Dosing Tables

Approved regimens are label-grade and prescribable within indication. Reference (non-approved) ranges are commonly cited compounding/literature figures, included for recognition only — not endorsements, and not validated protocols. Verify all dosing against current product labeling before prescribing.

Drug (Brand)	Route / Freq	Titration	Max / Maintenance
Semaglutide (Wegovy)	SC weekly	0.25 → 0.5 → 1.0 → 1.7 → 2.4 mg (q4 weeks)	2.4 mg
Semaglutide (Ozempic)	SC weekly	0.25 (×4 wk) → 0.5 → 1.0	up to 2.0 mg
Semaglutide (Rybelsus)	Oral daily	3 mg (×30 d) → 7 mg	14 mg
Tirzepatide (Zepbound/Mounjaro)	SC weekly	2.5 (×4 wk) → 5, then +2.5 q≥4 wk	5 / 10 / 15 mg (max 15)
Liraglutide (Saxenda)	SC daily	0.6 → 1.2 → 1.8 → 2.4 → 3.0 mg (weekly steps)	3.0 mg · reassess 16 wk (stop if <4%)
Liraglutide (Victoza)	SC daily	0.6 (×1 wk) → 1.2	max 1.8 mg
Dulaglutide (Trulicity)	SC weekly	0.75 → 1.5 → 3.0 → 4.5 mg (q≥4 wk)	4.5 mg
Exenatide (Byetta)	SC twice daily	5 → 10 mcg	10 mcg BID
Exenatide (Bydureon BCise)	SC weekly	Fixed	2 mg

Table A1 — Metabolic / Weight-Loss Peptides (FDA-Approved)

Peptide	Status	Route / Freq	Dose
Tesamorelin (Egrifta)	Approved (HIV lipodystrophy)	SC daily	2 mg
Sermorelin	Reference (non-approved)	SC nightly	~0.2–0.3 mg
CJC-1295 (no DAC) + Ipamorelin	Reference (non-approved)	SC nightly	~100 mcg each
MK-677 (ibutamoren)	Reference (non-approved; small molecule)	Oral daily	~10–25 mg

Table A2 — GH-Axis Peptides

Peptide	Status	Route / Freq	Dose
PT-141 (Vyleesi)	Approved (premenopausal HSDD)	SC PRN	1.75 mg, ~45 min before; max 1/24h, 8/month
BPC-157	Reference (non-approved)	SC 1–2×/day	~250–500 mcg
TB-500	Reference (non-approved)	SC	~2–2.5 mg 2×/wk loading → weekly
Thymosin α-1	Reference (non-approved in US)	SC 1–2×/wk	~1.6 mg
Epitalon	Reference (non-approved)	SC daily, cycled	~5–10 mg/day, short courses
Semax	Reference (non-approved)	Intranasal daily	Varies widely
Selank	Reference (non-approved)	Intranasal daily	Varies widely

Table A3 — Recovery, Sexual Health, Cognitive & Longevity Peptides

Peptide	Use	Typical Form
GHK-Cu	Skin firmness, hair-adjunct	Topical serum ~1–2 mg/mL, 1–2×/day
Matrixyl (palmitoyl pentapeptide-4)	Wrinkle/collagen support	Topical, pre-diluted, 1–2×/day
Argireline (acetyl hexapeptide-8)	Expression-line softening	Topical, 1–2×/day
PTD-DBM	Hair (experimental)	Topical/microneedling (no established dose)

Table A4 — Skin & Hair Peptides (Topical / Cosmetic)

The Three Dosing Formulas

- Concentration (mg/mL) = peptide (mg) ÷ water added (mL)
- Volume to draw (mL) = dose ÷ concentration
- Units (insulin syringe) = volume (mL) × 100

Back Matter

Peptide Status-at-a-Glance Chart

One row per peptide. This table doubles as the evidence-spectrum reference. "Snapshot only — verify current status before prescribing."

Peptide	FDA Status	Category 2 / Compounding	WADA	Evidence Tier
Semaglutide	Approved	N/A (approved drug)	Not prohibited	Proven
Tirzepatide	Approved	N/A	Not prohibited	Proven
Liraglutide	Approved	N/A	Not prohibited	Proven
Dulaglutide	Approved	N/A	Not prohibited	Proven
Pramlintide	Approved	N/A	Not prohibited	Proven
Tesamorelin	Approved (narrow)	N/A	Prohibited (S2)	Proven (indication)
PT-141 (bremelanotide)	Approved (narrow)	N/A	Not prohibited	Proven (indication)
Thymosin α-1	Not approved (US); approved abroad	Compounded	Check status	Plausible–proven (abroad)
CJC-1295	Not approved	Category 2 / review	Prohibited (S2)	Plausible
Ipamorelin	Not approved	Category 2 / review	Prohibited (S2)	Plausible

Table B1 — Status & Evidence Tier

Peptide	FDA Status	Category 2 / Compounding	WADA	Evidence Tier
Sermorelin	Not approved	Compounded	Prohibited (S2)	Plausible
Semax	Not approved (US)	Gray market	Check status	Plausible
Selank	Not approved (US)	Gray market	Check status	Plausible
BPC-157	Not approved	Category 2 / review	Prohibited (S0)	Plausible mechanism / hype outcomes
TB-500	Not approved	Category 2 / review	Prohibited (S0)	Plausible mechanism / hype outcomes
MK-677 (ibutamoren)	Not approved (not a peptide)	N/A	Prohibited (S2)	Plausible biomarker / unproven
AOD-9604	Not approved	Gray market / review	Check status	Hype
MOTS-c	Not approved	Gray market	Check status	Hype
Epitalon	Not approved	Gray market	Check status	Hype
5-Amino-1MQ	Not approved (not a peptide)	Gray market	Check status	Hype
GHK-Cu	Not a drug (cosmetic)	Topical / compounded	Topical: not prohibited	Plausible (cosmetic)
Matrixyl	Cosmetic ingredient	Topical	Not prohibited	Plausible (cosmetic)
Argireline	Cosmetic ingredient	Topical	Not prohibited	Plausible (cosmetic)
PTD-DBM	Not approved (experimental)	Gray market	Check status	Hype / experimental

Table B1 — Status & Evidence Tier

Back Matter

Anti-Doping Quick Reference (WADA)

Any patient subject to drug testing — competitive sport, military, or employer — changes the calculus entirely. Most peptides in this book are prohibited, and "recovery" or "wellness" use is not an exemption.

Prohibited Classes That Capture Peptides

- **S0 — Non-Approved Substances.** A catch-all that captures any substance not approved for human therapeutic use — e.g., BPC-157 and TB-500. If it isn't an approved human drug, assume it's prohibited.

- **S2 — Peptide Hormones, Growth Factors, Related Substances and Mimetics.** Captures GH secretagogues and GHRH analogs — CJC-1295, ipamorelin, sermorelin, GHRP-2/6, MK-677, tesamorelin. Many are banned at all times, in and out of competition.

The Athlete Screening Question

Ask **every** recovery, performance, or GH-axis candidate:

"*Are you subject to drug testing — for sport, the military, or your employer?*"

If **yes**, these peptides are off the table. **Document the question and the answer.**

Key Points for the Tested Patient

- Detection is real — WADA labs test for these peptides and their metabolites. Sellers' "undetectable" claims are marketing, not fact.
- A Therapeutic Use Exemption (TUE) is rarely granted for non-approved, unproven peptides — do not assume one will cover a compounded peptide.
- Redirect tested athletes to proven, permitted recovery: load management, physiotherapy, sleep, nutrition, and approved care.

Prescriber Liability

Providing — or even advising on — a prohibited substance for a tested athlete can carry professional, contractual, and legal consequences for you, not only the athlete. Screen, decline where appropriate, and document every conversation.

Back Matter

Glossary

503A pharmacy — Traditional compounding pharmacy preparing patient-specific medications under a valid prescription; primarily state-board overseen.

503B outsourcing facility — FDA-registered, cGMP-compliant facility that compounds in batches without patient-specific prescriptions.

Agonist — A molecule that binds and activates a receptor, mimicking the natural signal. (Antagonist = binds and blocks.)

Amylin analog — A peptide mimicking amylin, a satiety hormone co-secreted with insulin (e.g., pramlintide, cagrilintide).

Angiogenesis — Formation of new blood vessels; aids healing but also supports tumor growth.

Bioavailability — The fraction of an administered dose reaching systemic circulation in active form.

Bacteriostatic water — Sterile water with 0.9% benzyl alcohol that resists microbial growth; preferred for multi-dose reconstitution.

Biomarker — A measurable biological signal (e.g., IGF-1 level); distinct from a clinical outcome.

Category 2 — FDA designation for bulk substances with safety concerns that preclude compounding ("do not compound").

Certificate of Analysis (CoA) — Lab document verifying a product's identity, purity, and sterility.

cGMP — Current Good Manufacturing Practice; manufacturer-grade quality standards.

DAC (Drug Affinity Complex) — A modification that extends a peptide's half-life; CJC-1295 "with DAC" is long-acting (sustained), "without DAC" is short-acting (pulsatile).

GHRH — Growth hormone–releasing hormone; stimulates pituitary GH release. GHRH analogs: sermorelin, CJC-1295, tesamorelin.

GHRP / secretagogue — Growth hormone–releasing peptide / ghrelin mimetic; amplifies GH release via the ghrelin pathway (e.g., ipamorelin).

GLP-1 / GIP — Incretin gut hormones that amplify insulin release; the targets of metabolic peptides.

Half-life — Time for a drug's plasma concentration to fall by half; governs dosing frequency.

HSDD — Hypoactive sexual desire disorder; PT-141's approved indication (premenopausal women).

IGF-1 — Insulin-like growth factor 1; the downstream mediator of GH effects and the anchor lab for GH-axis monitoring.

Incretin effect — The amplified insulin response to oral (vs. IV) glucose, mediated by GLP-1 and GIP.

Lipohypertrophy — Lumps of thickened tissue from repeated same-site injection, causing erratic absorption.

Lyophilized — Freeze-dried; the form in which most peptides are supplied, requiring reconstitution.

Matrikine — A peptide fragment that signals collagen/matrix synthesis (e.g., Matrixyl).

MEN-2 — Multiple endocrine neoplasia type 2; with medullary thyroid carcinoma, an absolute contraindication to GLP-1 agents.

Pulsatile vs. sustained signaling — Whether a peptide preserves the body's natural rhythmic hormone release (pulsatile) or flattens it into continuous elevation (sustained).

Reconstitution — Dissolving a lyophilized peptide in diluent before use.

"Research Use Only" — A gray-market label that is a legal workaround, not a safety designation.

Subcutaneous (SC) — Injection into the fat layer beneath the skin; the default peptide route.

TUE — Therapeutic Use Exemption; permits an otherwise-prohibited substance under anti-doping rules.

WADA — World Anti-Doping Agency; sets the prohibited-substance list for sport.

Back Matter

How to Verify Current FDA and WADA Status

Because regulatory status is a snapshot, verification is a recurring duty, not a one-time check. A practical routine:

For FDA approval and labeling

- Confirm a drug's approval and current prescribing information via the FDA's official drug databases (Drugs@FDA) and the product label.
- For compounding eligibility, consult the FDA's bulk substances lists and the relevant 503A/503B guidance, and watch for proposed rules and notices.
- For shortage-dependent compounding, check the current FDA drug shortage list — status can change the legality of compounding.

For compounding-review status

- Track FDA advisory committee (e.g., PCAC) agendas and outcomes for peptides under review (BPC-157, TB-500, and others).
- Treat "under review" as a moving target — re-check before each prescribing cycle.

For anti-doping status

- Check the current WADA Prohibited List (updated at least annually) and the relevant national anti-doping organization.
- Use the sport-specific "check your substance" resources where available.

Build it into practice

- Assign responsibility for monitoring FDA / Category 2 / WADA changes.
- Schedule periodic protocol and consent reviews.
- Re-verify any specific status in this book before acting on it — every status statement here reflects a particular moment.

Back Matter

Key References

This handbook synthesizes peer-reviewed literature, FDA regulatory materials, and product labeling. The following categories represent the primary source types underpinning the text; consult the current versions, as all are subject to update.

Pivotal clinical trials (metabolic)

- STEP 1 trial — semaglutide for weight management (New England Journal of Medicine, 2021).
- SURMOUNT-1 trial — tirzepatide for weight management (New England Journal of Medicine, 2022).
- RECONNECT trials — bremelanotide (PT-141) for HSDD.
- Saxenda (liraglutide) and Egrifta (tesamorelin) Phase III programs.

Evidence reviews

- Systematic review of BPC-157 (2025) — screening and inclusion data establishing the predominance of preclinical evidence.
- Reviews of AOD-9604 development, including the failed pivotal trial and 2007 termination.
- Reviews of GH-axis peptides and IGF-1/cancer epidemiology.

Regulatory sources

- FDA: Drugs@FDA; compounding (503A/503B) guidance and bulk substances lists; drug shortage list; advisory committee (PCAC) materials.
- Current FDA-approved product labeling for all approved agents cited.

Anti-doping

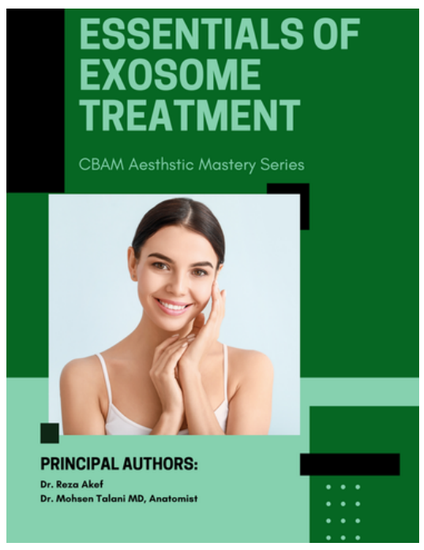
- WADA Prohibited List (current annual edition) and classification documents.

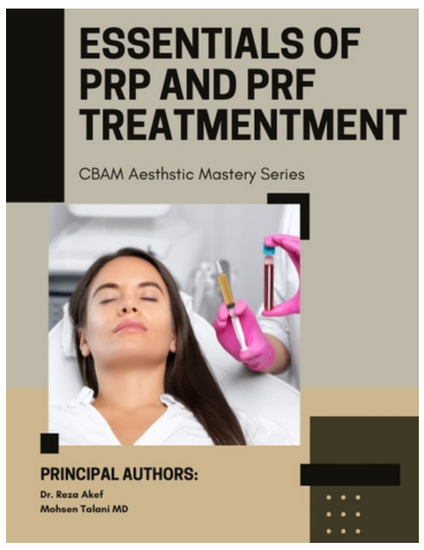
Professional and safety guidance

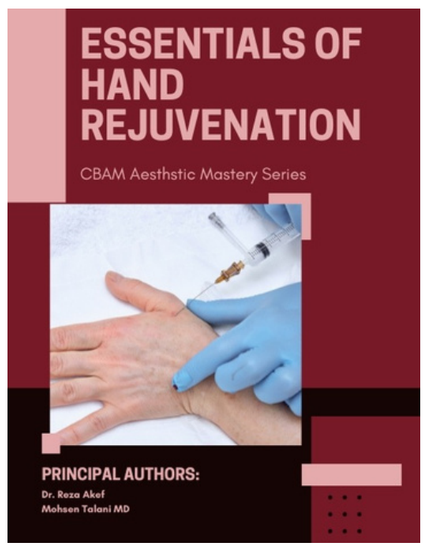
- ASA/ASRA guidance on GLP-1 receptor agonists and peri-procedural management.
- Relevant professional-society statements on obesity pharmacotherapy and compounded peptides.

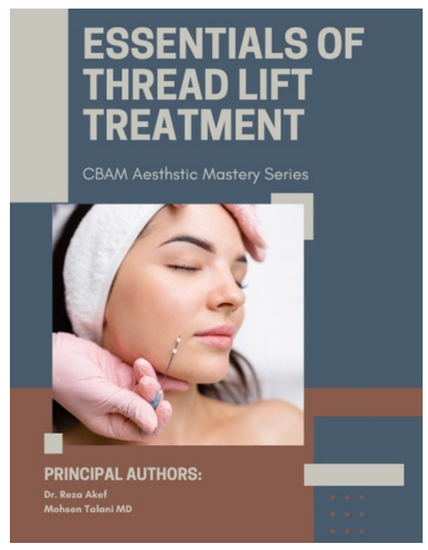
For all dosing, status, and safety information, the current product label and current regulatory and anti-doping sources supersede any statement in this handbook.

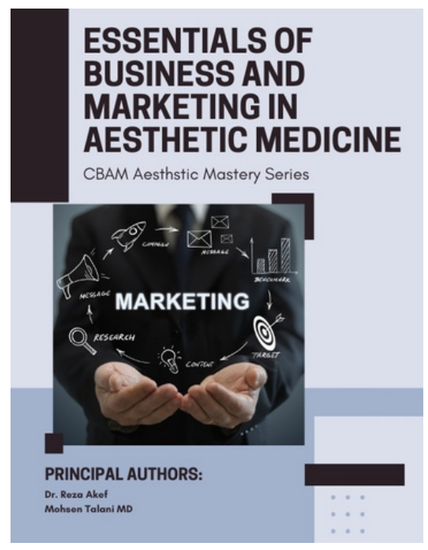
CBAM Aesthetic Mastery Series

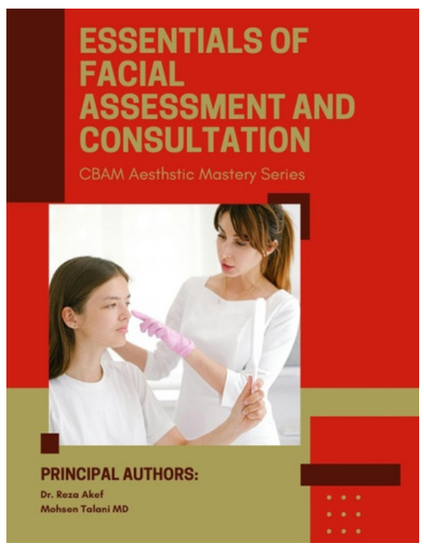


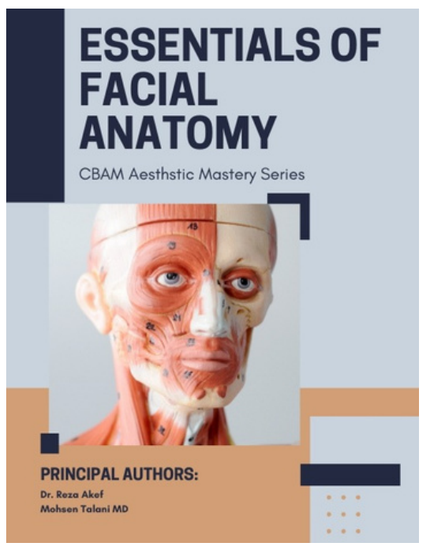




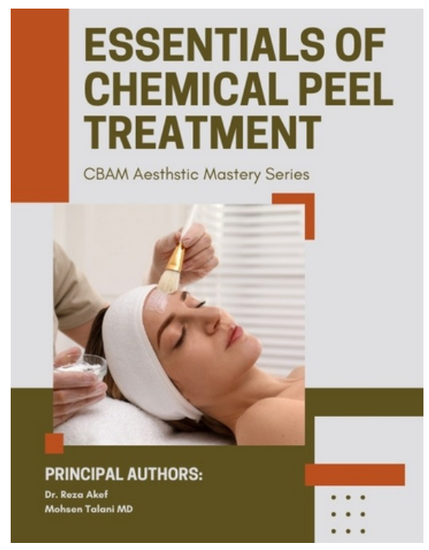


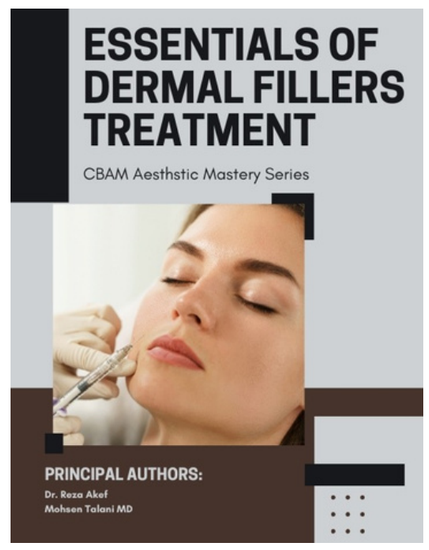












Principal Authors:



Dr. Reza Akef

MD, CCFP-EM

Dr. Reza Akef is a highly experienced and respected cosmetic physician, with over 15 years of experience in teaching and practicing cosmetic medicine. He is currently the Assistant Professor at McMaster University and the Chairman of the Canadian Board of Aesthetic Medicine (CBAM), where he shares his knowledge and expertise with other healthcare professionals to provide the best care for their patients. Dr. Akef is board certified by the College of Family Physicians of Canada in both Family and Emergency Medicine. Additionally, he is deeply involved in interventional pain practice cooperation for the treatment of Migraines, chronic pain, TMJ, Myofascial pain, and Fibromyalgia.



Dr. Mohsen Talani

MD, Anatomist

Mohsen Talani is the Director of CBAM. He has over 18 years of experience teaching anatomy in Canada and internationally to students and healthcare practitioners in different fields of medicine such as physicians, dentists, nurses, chiropractors, and physiotherapists.
After graduating from medical school at a young age, he became a medical doctor in his home country, Iran, and practiced in the field of emergency medicine. While pursuing his Master's thesis in neuroscience at McGill University, he discovered his passion for teaching. Since then, he has been working in the field of medical science education, with a focus on anatomy.

ISBN 978-0-7334-2609-4
9780733426094

CBAM Publications
www.CBAMedicine.com

CBAM PUBLICATIONS
Canadian Board of Aesthetic Medicine