

## Leuphasyl — Basic Review Questions

1. What is Leuphasyl, what type of peptide is it, and what is its regulatory status?

Answer: Leuphasyl is the trade name for Pentapeptide-18, a topical cosmetic peptide made of five amino acids. It is described as a “Botox-mimetic” — a synthetic mimic of the body’s own opioid neuropeptide (Leu-enkephalin) — used in serums and creams to soften expression wrinkles. Unlike most peptides in this series, it has no injectable or systemic use; it is applied to the skin only. It is not an FDA-approved drug but is regulated as a cosmetic ingredient, legal as long as no drug or mechanistic claims are made.

2. How does Leuphasyl work?

Answer: It mimics Leu-enkephalin and binds the delta-opioid receptor on the nerve endings that signal facial muscles to contract. Activating that receptor closes calcium channels in the nerve terminal, and without that calcium signal the nerve releases less acetylcholine — the chemical that tells muscle to contract. With less acetylcholine, the muscle contracts more weakly, and with repeated use over weeks the expression lines those muscles create become softer. Importantly, it modulates (reduces) acetylcholine rather than blocking it, and the effect is fully reversible.

3. How does Leuphasyl differ from Argireline and from Botox?

Answer: All three relax facial muscle by reducing acetylcholine release, but they hit different steps of the same cascade. Leuphasyl acts upstream — at the calcium trigger for acetylcholine release. Argireline acts midstream, interfering with the SNARE/SNAP-25 machinery that lets the nerve release acetylcholine. Botox acts by enzymatically cutting SNAP-25, fully blocking release for months. Leuphasyl and Argireline only modulate release and are fully reversible, making them far milder than Botox. Because Leuphasyl and Argireline target different steps, combining them is synergistic — they do more together than either alone.

4. What is Leuphasyl’s signature use, and how should it be applied?

Answer: Its signature use is the combination with Argireline, marketed as “Argirelox” — pairing an upstream and a midstream muscle-relaxing peptide produced greater wrinkle reduction than either alone. It also complements GHK-Cu, the other Skin Resilience peptide: GHK-Cu rebuilds the collagen/elastin matrix (the “canvas”) while Leuphasyl relaxes the muscles that crease it, so the two are often paired. Two practical points: only the roughly 2% concentration produced a meaningful effect in testing, and it should be applied across the whole expression-muscle area (forehead, frown, crow’s feet) — not just on the visible line — because the target is the muscle.

5. What is the state of the evidence, and what is the central uncertainty?

Answer: The mechanism is well demonstrated in laboratory (in vitro) studies, but the efficacy evidence is weak: all the human anti-wrinkle data come from manufacturer-sponsored, open-label studies, with no randomized placebo-controlled trials and no independent replication. The reported roughly 28–35% wrinkle reduction at 2% over 60 days is encouraging for a topical, but the central unanswered question is

whether a topically applied peptide actually penetrates deeply enough to reach the motor-nerve terminals at a meaningful concentration. There are no skin-penetration or pharmacokinetic studies, so it is genuinely unclear how much of the effect is the peptide versus the formulation itself.

6. What is the safety profile, and how should expectations be set?

Answer: Short-term topical safety looks reassuring: in cosmetic testing it showed no cytotoxicity, no genotoxicity, no eye or skin irritation, and excellent skin compatibility. The limits are that there is no data on systemic absorption, no evaluation beyond about 60 days of use, and no data in pregnancy or lactation, so it should be avoided in pregnancy and on broken or inflamed skin. Expectations should be set modestly — it produces a gradual, reversible softening of expression lines and is not a substitute for injectable Botox in degree or duration. It is best framed as a low-risk, needle-free cosmetic adjunct; if combined with Botox, watch for excessive muscle relaxation.