

# Epitalon (AEDG)

Sleep Hygiene — Review Questions

Six open-response questions covering identity, mechanism, clinical use and dosing, why Epitalon belongs in the sleep-hygiene toolkit, key limitations, and safety. Model answers are drawn strictly from the lecture and slides.

## 1. Identity & status: What is Epitalon, and how does its regulatory standing differ from that of Epithalamin?

### Answer

Epitalon is a **synthetic pineal tetrapeptide, Ala-Glu-Asp-Gly (AEDG, ~390 Da)** — the single defined active sequence distilled from the crude bovine pineal extract **Epithalamin**, and developed by Prof. Vladimir Khavinson's St. Petersburg institute. It is classified as a pineal bioregulatory peptide and geroprotector. The key distinction is that the two are **not interchangeable**: Epithalamin is a complex multi-peptide extract that is a **registered preparation in Russia** and carries the larger historical cohort dataset, whereas Epitalon is a single reproducible synthetic peptide that is **not on any official drug registry — including Russia's** — and is used only within certain institutes under research protocols. Epitalon is not FDA- or EMA-approved; all human use is **experimental and off-label**, requiring documented informed consent.

## 2. Mechanism: What is Epitalon's mechanistic basis for use in sleep, and what are its broader actions?

### Answer

The sleep rationale is the pineal–melatonin axis. Epitalon **upregulates AANAT** (the rate-limiting enzyme of melatonin synthesis) and **pCREB** in pinealocytes, **selectively protects aged pinealocytes**, and **modulates the molecular clock** in human leukocytes (Clock decreased ~1.8-fold, Cry2 roughly doubled). In elderly humans, 0.1 mg normalized melatonin as effectively as 50 mg of Epithalamin — so a **low evening dose** raises the body's own melatonin output rather than supplying it exogenously. Beyond sleep, the lecture frames Epitalon as a **master epigenetic regulator** acting across six interconnected pathways: it **reactivates telomerase (hTERT)** in normal cells (26-fold in HMEC), binds linker histones (H1/6, H1/3) to **decondense heterochromatin** for transcription, upregulates **antioxidant enzymes** (SOD, glutathione peroxidase), increases **neurogenic markers** and reduces 8-OHdG (DNA-damage protection), and shows **anti-tumor activity** in rodents. For sleep specifically, the operative levers are melatonin output, circadian-clock modulation, and downstream NAD mechanisms.

## 3. Clinical use & dosing: How is Epitalon dosed for sleep, and how does that relate to the other regimens?

### Answer

For sleep, the relevant regimen is the **low-dose nighttime protocol: ~100–300 µg (300 µg is the practical standard) taken at night** to raise melatonin output and support the circadian clock and downstream NAD mechanisms. This range derives from a mouse→human translation (~2.4 µg/kg, i.e. ~170–200 µg for a 70–90 kg person); ~100 µg daily for 10 days approximates the original Epithalamin study translation. Two other regimens exist but are not the sleep approach: **continuous daily** (~3 mg/day, cycled roughly 3 months on / ~6 weeks off) and **high**

“**mega**” dosing (5–10 mg/day SC over 10–20 days, 2–3 cycles/year), the legacy Epithalamin-derived longevity protocol. All dosing is **empirical and off-label**; evening administration is preferred for melatonin synergy; reconstitute with bacteriostatic water and **do not shake**. The key potency anchor is that 0.1 mg of Epitalon equals ~50 mg of Epithalamin for melatonin normalization. Epitalon is best used as an **adjunct within a sleep-hygiene program**, not as a standalone hypnotic.

#### 4. The defining question: Why does Epitalon belong in the sleep-hygiene toolkit, and how should it be positioned relative to behavioral sleep hygiene and to melatonin supplementation?

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##### Answer

Epitalon belongs in the sleep group because it acts on the **upstream machinery of sleep**: rather than supplying melatonin from outside, it drives the **pineal gland's own melatonin production** (via AANAT/pCREB upregulation) and modulates the circadian clock (Clock down, Cry2 up). Dosed at night, that translates into higher nocturnal melatonin, better sleep, and support for the nighttime recovery and NAD processes that depend on an intact melatonin rhythm — which is why Dr. Seeds reports the **300 µg nighttime dose** as effective for sleep, and notes benefit in poor-sleep, post-COVID, and post-Lyme fatigue states. On positioning: it is a **mechanistic adjunct, not a primary hypnotic and not a substitute for foundational sleep hygiene and behavioral measures**, which carry stronger evidence and (per the lecture) should be addressed first. It also differs from melatonin supplementation in kind — restoring endogenous output and circadian signaling rather than replacing the hormone — which is the conceptual basis for combining evening Epitalon with sleep-aligned behavioral changes.

#### 5. Key limitation: Given thousands of patients dosed over many years, why isn't that a validated evidence base — and what is the historical sourcing story?

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##### Answer

Because that experience is **uncontrolled and single-source**, and partly the product of a labeling error. Dr. Seeds recounts the early “Wild West” era when product sold as **Epitalon was frequently Epithalamin (and vice versa)**; to avoid harm, he kept the established high-dose Epithalamin protocol (~50–100 mg over 10 days) in play, which is why “Epitalon” was dosed very high for years. Across thousands of such patients he observed **no safety signals or immune toxicities**, and reported notable benefit in **post-COVID and post-Lyme chronic fatigue and neurocognitive presentations** at those higher doses. That is genuinely useful real-world context — but it is **not validated trial evidence**. Essentially all data come from the Khavinson group without independent replication; there are no Phase I–III trials, no human PK, and the strongest outcomes come from **multi-agent regimens** (e.g., Thymalin + Epitalon) that make single-agent attribution impossible. The appropriate stance is meticulous documentation while awaiting proper trials.

#### 6. Safety & monitoring: How should Epitalon be screened, monitored, and positioned — and what is the key takeaway?

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##### Answer

The hard safety rule comes from a mechanistic split: in **normal cells** telomeres lengthen via canonical **telomerase (hTERT) activation**, but in **cancer cells** they lengthen via **ALT**

**(Alternative Lengthening of Telomeres)** with rising hTERT mRNA — a theoretical, unproven oncogenic signal. Because of it, **cancer screening is the non-negotiable first step**, and any active or historical malignancy is an **absolute contraindication** (along with pregnancy/lactation and pediatric use); relative contraindications include strong family cancer history, telomerase-driven cancers, concurrent oncologic agents, and uncontrolled systemic illness, with uncharacterized interactions for immunosuppressants, anticoagulants, and mTOR inhibitors. **Monitoring** runs baseline (cancer screening first, melatonin and inflammatory markers, telomere length if available) → cycle-end (sleep quality, injection site, tolerability) → 3 months (immune panels, hormones, inflammatory markers) → annual (serial telomere/methylation clock of limited utility, cancer surveillance). **Positioning for sleep:** a low-dose evening **adjunct within a sleep-hygiene program**, presented as a research-stage peptide — never a validated therapy — used investigationally with full informed consent. **Key takeaway:** a broad-acting synthetic pineal tetrapeptide that, for sleep, drives endogenous melatonin at a low nighttime dose, defined apart from Epithalamin, but supported only by preclinical-grade evidence and carrying a signature ALT-in-cancer caution that makes cancer screening mandatory and malignancy a contraindication.

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*For educational and research purposes only. Not medical advice. Epitalon (AEDG) is NOT FDA- or EMA-approved and is not on any official drug registry, including Russia. All human use is experimental and off-label; there are no Phase I–III trials or human pharmacokinetic data, and an ALT signal in cancer cells makes cancer screening mandatory and malignancy history a contraindication. Based on lecture materials by William Seeds, MD — SSRP Institute | Cellular Medicine Education.*