RonanRx
PERSONALIZED MEDICINE

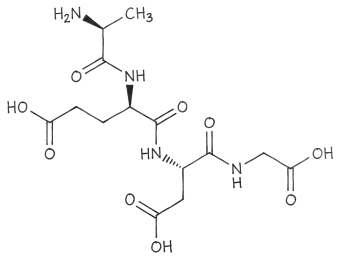
CLINICAL MONOGRAPH · METABOLIC & LONGEVITY (UNDER FDA REVIEW)

Epitalon / Epithalon

Pineal peptide research ingredient with physician-request review

Epitalon (also spelled epithalon) is a short four-amino-acid synthetic peptide, Ala-Glu-Asp-Gly, that was proposed by a Russian research group at the St. Petersburg Institute of Bioregulation and Gerontology in the 1990s as a synthetic equivalent of an older bovine pineal-gland extract called 'epithalamin'. Russian researchers, led by Vladimir Khavinson and Vladimir Anisimov, have published a series of laboratory and animal studies arguing that epitalon increases telomerase activity, extends lifespan in mice, and slows certain age-related changes [khavinson2003_telomerase; anisimov2003_lifespan].

Epitalon has no FDA approval in the United States. This ingredient is part of an evolving FDA review process. Physicians may submit patient-specific prescription requests for pharmacy review. Availability is determined case by case, and availability may change after FDA review, PCAC discussion, final agency action, or state-board guidance.



EVIDENCE POSTURE PRECLINICAL

REVIEWED **2026-05-11**

State-licensed 503A | Pharmacist reviewed | Doctor led | Cold-chain ready | Patient choice preserved

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FOR CLINICIANS

Epitalon is a synthetic tetrapeptide Ala-Glu-Asp-Gly (AEDG) developed by the St [djeridane2003_melatonin]. Petersburg Institute of Bioregulation and Gerontology as a proposed active-fragment synthetic analog of the bovine pineal polypeptide preparation 'epithalamin' used in Soviet and post-Soviet Russian clinical research from the 1980s [khavinson2017_aedg]. The discovery-era hypothesis, articulated in Bulletin of Experimental Biology and Medicine and Neuroendocrinology Letters [khavinson2002_chromatin, khavinson2003_telomerase, khavinson2003_transcription], proposes that the AEDG sequence penetrates the nucleus, binds to gene-promoter sites, and modulates transcription of aging-related genes including the catalytic subunit of telomerase. Preclinical work by the same group has characterized AEDG effects on chromatin activation in aged cells, on melatonin synthesis in pineal organotypic culture, on rodent immune and reproductive endocrinology, and on lifespan in mouse aging models [khavinson2012_pineal_culture].

Human clinical evidence is largely confined to a series of Russian-language reports from the Korkushko group in Kiev and the Khavinson group in St. Petersburg, including a 15-year geroprotective follow-up of elderly subjects receiving the older bovine peptide preparation 'epithalamin' (not the synthetic tetrapeptide) [korkushko2011_15year] and shorter-term work reporting modulation of melatonin circadian rhythm and immune/endocrine measures in elderly patients [korkushko2004_melatonin, korkushko2006_geroprotective, labunets2007_chronic_cad]. These reports are small, predominantly open-label, conducted at single Russian and Ukrainian centers, and have not been independently replicated in Western clinical research. There is no FDA approval, no FDA-reviewed clinical pharmacology, no Western randomized controlled trial of the synthetic AEDG tetrapeptide in any indication, and no pharmacovigilance database. A 2025 narrative overview in International Journal of Molecular Sciences [araj2025_overview] catalogs the AEDG literature and similarly emphasizes the dependence of the evidence base on the Khavinson group's preclinical and small-clinical reports [anisimov2003_lifespan; anisimov2003_carcinogenesis]. Mechanistic claims about telomerase activation and telomere lengthening have recently been re-examined in a single 2025 cell-line report in Biogerontology [shamporov2025_telomere] (subsequently issued an Erratum-style correction [shamporov2025_correction]); independent confirmation in primary human tissues remains absent [semenchenko2004_lifespan].

Epitalon has no FDA approval in the United States. This ingredient is part of an evolving FDA review process. Physicians may submit patient-specific prescription requests for pharmacy review. Availability is determined case by case, and availability may change after FDA review, PCAC discussion, final agency action, or state-board guidance.

Why Personalized Epitalon / Epithalon

The evidence base for Epitalon is limited and uneven. It includes Russian and preclinical work around pineal peptides, sleep, and cellular aging markers, but no FDA-reviewed clinical program establishes an approved US indication.

Physicians may submit patient-specific prescription requests for Epitalon for pharmacy review. Certain preparations may be available now when clinically appropriate, lawfully prescribed, supported by patient-specific documentation, and approved by the dispensing pharmacy. Availability is determined case by case. This is not a consumer access promise; it is a clinical, sourcing, formulation, and regulatory review process. FDA has scheduled Epitalon-related bulk drug substances for discussion at the 23-24 Jul 2026 Pharmacy Compounding Advisory Committee meeting.

For Epitalon, the patient-specific route matters because consumer marketing often turns thin evidence into broad longevity claims. RonanRx review keeps the request tied to a licensed prescriber, a named patient, and pharmacist judgment.

Quick Facts About Epitalon / Epithalon

Category: Synthetic tetrapeptide Ala-Glu-Asp-Gly (AEDG), proposed pineal-gland analog modeled on the bovine pineal polypeptide preparation 'epithalamin'

Active ingredient: Epitalon (also written 'epithalon', 'epitalone', or AEDG peptide), a four-amino-acid sequence Ala-Glu-Asp-Gly. The peptide is structurally distinct from, but pharmacologically proposed as the active fragment of, the older bovine-derived pineal polypeptide preparation 'epithalamin' used in Russian clinical research from the 1980s onward.

FDA-approved branded forms: None. Epitalon has no FDA-approved indication, no approved branded product, and no NDA, ANDA, or BLA history in the United States.

Route: Intramuscular and subcutaneous injection in Russian-language clinical and preclinical reports; intranasal in selected rodent neurophysiology studies

Evidence posture: Preclinical only. Almost all primary literature is authored by the Khavinson group at the St. Petersburg Institute of Bioregulation and Gerontology and published in Russian-language journals (Advances in Gerontology, Bulletin of Experimental Biology and Medicine, Voprosy Onkologii) or Eastern European outlets. There is no independent Western replication of the telomerase, lifespan-extension, or anti-aging findings, no Western-conducted randomized controlled trial, and no FDA-reviewed clinical pharmacology dataset.

FDA-approval status: Category 2, evolving FDA review process. Valid patient-specific prescription required; supporting clinical rationale may be requested.

Compounded under: Physicians may submit patient-specific prescription requests for pharmacy review. Availability is determined case by case.

Supply-chain caution: Most circulating 'epitalon' preparations are research-grade peptide manufactured outside any pharmaceutical-quality system. Analytical work by Esposito and colleagues identified epitalon in a research-grade peptide preparation and characterized it as a substance of potential abuse, underscoring the absence of identity, purity, sterility, and potency assurances in the unregulated market.

> **SPECIALS: PATIENT-SPECIFIC PRESCRIPTION ONLY**
>
> Physicians may submit patient-specific prescription requests for Epitalon / Epithalon for pharmacy review. Certain preparations may be available now when clinically appropriate, lawfully prescribed, and approved by the dispensing pharmacy. Availability is determined case by case.
>
> - **Made to order, not off a shelf.** No batch sits in a warehouse waiting for buyers. Your prescription triggers the prep.
> - **Named-patient label.** The bottle carries one patient's name. The batch records carry one prescription.
> - **Dose, strength, and route chosen for the patient.** A prescriber decides what gets compounded, not a manufacturer who set the strength for a trial population.
> - **Licensed pharmacist on the hook.** A real person, with a license that can be pulled, signs off on every prep. State inspectors check the facility.
> - **Compounded drugs are not FDA-approved.** They should not be evaluated using branded-drug trial data alone. Availability varies by state and prescribed medication.

How This Differs from a Research-Use-Only Website

A research-use-only website ships a vial from a warehouse. There is no prescription, no pharmacist, no facility inspection, and no way to recall the product if something is wrong with it. If the vial is mislabeled, contaminated, or under-potent, there is nobody whose license is at stake.

A 503A compounding pharmacy is the other thing. The doctor writes the prescription. A licensed pharmacist, whose name is on the label, prepares the medicine in a facility the state inspects. If something goes wrong, there is a person and a license on the hook, and a documented chain of custody on every lot. That accountability is what makes it safe.

What is Epitalon / Epithalon?

Epitalon is a synthetic linear tetrapeptide with the sequence Ala-Glu-Asp-Gly (alanine-glutamate-aspartate-glycine), commonly abbreviated AEDG. It was designed at the St. Petersburg Institute of Bioregulation and Gerontology under Vladimir Khavinson as the proposed minimal-active sequence of the older bovine pineal polypeptide preparation known in Russian-language literature as 'epithalamin' [khavinson2017_aedg, araj2025_overview]. The two preparations are pharmacologically distinct: 'epithalamin' is a complex

polypeptide mixture extracted from bovine pineal tissue and has been used in Russian and Ukrainian clinical research since the 1980s, while 'epitalon' / 'epithalon' is a chemically defined four-residue synthetic peptide.

Epitalon is most often described in published preclinical reports as administered by parenteral injection (intramuscular or subcutaneous) at microgram-to-low-milligram doses in rodent studies, with intranasal administration also reported in selected neurophysiology experiments [morozov2007_intranasal]. The synthetic peptide has been characterized by mass spectrometry in research-grade preparations [esposito2015_analytical, khavinson2017_aedg], confirming the four-residue identity. There is no FDA-approved finished drug product containing epitalon, no FDA-registered manufacturer, and no compendial USP monograph.

How Epitalon / Epithalon Works

The mechanistic hypothesis advanced by the Khavinson group proposes that epitalon is a short cell-penetrating peptide that crosses cell and nuclear membranes, binds to DNA at specific gene-promoter sites, and modulates the transcription of genes involved in aging, telomere maintenance, and pineal-gland endocrine function. Khavinson et al. (Bull Exp Biol Med, 2003) reported that AEDG induces telomerase activity and telomere elongation in cultured human somatic cells [khavinson2003_telomerase]. The same group has reported chromatin de-condensation effects in aged-cell models [khavinson2002_chromatin] and effects of short peptides on gene transcription in mouse heart and brain [khavinson2003_transcription, anisimov2004_brain_genes].

Additional preclinical work has reported binding of fluorescence-labeled short peptides to cell-penetrating tracks into the nucleus in HeLa cells and in vivo [fedoreyeva2011_penetration], DNA-double-strand melting after binding to the AEDG tetrapeptide [khavinson2008_dna], and signaling-molecule expression in organotypic pineal cell culture [khavinson2012_pineal_culture, khavinson2012_melatonin_mechanism]. Mechanistic claims about gene-promoter binding and telomerase induction have not been independently replicated in Western academic laboratories using contemporary chromatin-immunoprecipitation, biochemical-binding, or telomerase-assay methods, and the proposed sequence-specific DNA binding mode for a tetrapeptide as small as AEDG remains an unusual hypothesis from the standpoint of mainstream nucleic-acid pharmacology.

A 2025 cell-line study in Biogerontology [shamporov2025_telomere] re-examined the telomere-length effect in human cell lines, reporting telomerase upregulation; this paper was subsequently the subject of a published Correction [shamporov2025_correction]. The 2025 narrative overview by Araj and colleagues [araj2025_overview] summarizes the mechanistic literature and notes that the molecular pharmacology of epitalon remains poorly characterized relative to other peptides at comparable stages of investigational interest.

Biological Role of Epitalon / Epithalon

The biological framing advanced by the Khavinson group describes epitalon as a synthetic 'peptide bioregulator' that mimics the activity of the endogenous pineal-gland polypeptide complex known historically in Russian-language pharmacology as 'epithalamin'. The pineal gland produces melatonin and a constellation of peptide and protein factors involved in circadian-rhythm regulation, neuroendocrine signaling, and immune modulation; the Khavinson hypothesis posits that short pineal-derived peptides such as AEDG act as direct gene-expression modulators in addition to or independently of melatonin-axis effects [khavinson2003_telomerase, khavinson2017_aedg, araj2025_overview].

This framing is biologically narrower than the endocrine framing of established peptide therapeutics. Unlike incretin-axis peptides (which act through well-characterized GPCRs), thymic peptides (which act through immune-receptor pathways), or melanocortin peptides (which act through the melanocortin receptor family), AEDG has no identified high-affinity cell-surface receptor. The proposed direct gene-promoter binding by a four-residue peptide is a non-canonical pharmacological mode that has not been independently replicated using contemporary chromatin-immunoprecipitation, electrophoretic-mobility-shift, or surface-plasmon-resonance methods. The 2025 Araj overview and the 2026 Bagheri review acknowledge this gap [araj2025_overview, bagheri2026_gerontology].

Detailed Mechanism of Epitalon / Epithalon

The Khavinson 2003 paper in Bulletin of Experimental Biology and Medicine [khavinson2003_telomerase] is the foundational mechanistic report. The authors reported that incubation of cultured human fetal fibroblasts with the AEDG tetrapeptide produced detectable telomerase activity and an increase in mean telomere length, framed as a 'bioregulatory' effect of a short pineal-derived peptide on cellular aging. The assay methodology and the cell-line provenance reported in the paper are limited by current standards, and the result has not been independently reproduced in primary peer-reviewed cell biology literature outside the Khavinson group.

Follow-up reports from the same group extended the gene-regulatory hypothesis. Anisimov and Khavinson (Neuroendocrinology Letters, 2004) reported gene-expression effects of related short peptides in mouse heart and brain [anisimov2004_brain_genes, anisimov2004_heart_genes]. Khavinson and Shataeva (Bull Exp Biol Med, 2003) proposed that short regulatory peptides act at the transcriptional level [khavinson2003_transcription]. Khavinson, Solovyov, and Shataeva (Bull Exp Biol Med, 2008) reported DNA-double-strand melting after binding to a geroprotective tetrapeptide [khavinson2008_dna]. Linkova and colleagues described peptide-induced regulation of signaling molecules in organotypic pineal culture [khavinson2012_pineal_culture] and proposed molecular-cellular mechanisms of peptide regulation of melatonin synthesis [khavinson2012_melatonin_mechanism]. Linkova et al. (Adv Gerontol, 2012)

extended the immune-aging hypothesis to AEDG-interferon-gamma interactions in murine aging models [linkova2012_immune].

Independent identification work by the Khavinson group in 2017 [khavinson2017_aedg] used mass spectrometry to confirm the presence of the AEDG sequence in the polypeptide complex of the bovine pineal gland, work supporting the original 'active fragment' hypothesis linking the synthetic tetrapeptide to the bovine 'epithalamin' preparation used clinically in Russian and Ukrainian gerontology research from the 1980s onward. A more recent narrative review by Khavinson, Linkova, and colleagues [linkova2019_neurodifferentiation] and the 2025 Araj overview [araj2025_overview] summarize the proposed mechanism with the same caveat: independent biochemistry-laboratory replication of the gene-binding and telomerase-induction claims has not appeared in the indexed Western peer-reviewed literature.

Two more recent in-vitro reports from independent groups have engaged with the mechanism. Ashapkin and colleagues (Int J Mol Sci, 2020) reported that the AEDG peptide stimulates gene expression and protein synthesis during human fetal-cell senescence in vitro [ashapkin2020_senescence], and Shamporov et al. (Biogerontology, 2025) reported telomere lengthening in human cell lines through telomerase upregulation [shamporov2025_telomere], with a published Correction issued the same year [shamporov2025_correction]. A 2025 Stem Cell Reviews and Reports paper reported that epitalon enhances delayed wound healing in an in vitro model [pankov2025_wound]. These individual reports do not yet constitute the kind of mechanism-replication consensus that is available for clinically validated peptide therapeutics.

Epitalon / Epithalon Research History

Epitalon (epithalon, AEDG) was developed at the St. Petersburg Institute of Bioregulation and Gerontology by Vladimir Khavinson and colleagues as a proposed synthetic active fragment of the older bovine pineal polypeptide preparation 'epithalamin'. Epithalamin was used in Soviet and post-Soviet Russian and Ukrainian clinical research from the 1980s onward as a geroprotective agent under Russian Ministry of Health authorization, principally in elderly patients with cardiovascular and metabolic conditions [korkushko2011_15year] [vinogradova2007_muscles; ilina2009_antiox]. The synthetic AEDG tetrapeptide was advanced in the 1990s and 2000s as a chemically defined alternative to the polypeptide mixture.

Foundational preclinical reports from the Khavinson group through 2002, 2008 characterized AEDG effects on chromatin in aged cells [khavinson2002_chromatin], on telomerase activity and telomere length in cultured human somatic cells [khavinson2003_telomerase], on melatonin secretion in young and old rats and in pineal-cell culture [djeridane2003_melatonin, khavinson2012_pineal_culture], on lifespan and spontaneous tumor incidence in Swiss-derived SHR mice [anisimov2003_lifespan], on transgenic HER-2/neu mice [anisimov2002_her2, semenchenko2004_lifespan], on female-rat lifespan under different light regimes [anisimov2007_lifespan], on colon carcinogenesis in rats [kossoy2003_colon], and on

spontaneous carcinogenesis in senescence-accelerated SAM mice [anisimov2003_carcinogenesis]. Reports of broader immune, endocrine, and stress-axis effects of short peptides on rodent aging followed [labunets2003_thymocyte; kazakova2005_il2; linkova2012_immune].

Clinical work in humans is largely confined to small Russian-language reports from the Korkushko group at the D.F. Chebotarev Institute of Gerontology in Kiev, Ukraine. Korkushko, Khavinson, Shatilo, and Magdich (Bull Exp Biol Med, 2004) reported that the bovine peptide preparation epithalamin restored circadian melatonin rhythm in elderly subjects [korkushko2004_melatonin]; the same group reported geroprotective effects on accelerated-aging elderly subjects in 2006 [korkushko2006_geroprotective] and a 15-year follow-up summary of repeated epithalamin courses in elderly patients in 2011 [korkushko2011_15year]. Labunets and colleagues reported effects on circadian rhythm of immune and endocrine functioning in patients with chronic coronary artery disease (Bull Exp Biol Med, 2007) [labunets2007_chronic_cad]. These reports are small, predominantly open-label, conducted at one or two collaborating centers, and have not been independently replicated outside the Russian/Ukrainian academic network.

Independent Western engagement with the molecule is limited. Esposito et al. (Drug Testing and Analysis, 2015) identified epitalon in research-grade peptide preparations and characterized it as a substance of potential abuse [esposito2015_analytical]. The 2025 narrative overview by Araj et al. in Int J Mol Sci [araj2025_overview] and a 2026 peptide-therapeutics review in Frontiers in Aging [bagheri2026_gerontology] catalog the AEDG literature. A 2022 Aging (Albany NY) paper from an independent group reported a protective effect of epitalon on post-ovulatory aged mouse oocytes in vitro [yang2022_oocyte], and a 2025 Stem Cell Reviews and Reports paper reported wound-healing effects in an in vitro model [pankov2025_wound]. A small 2025 Life Sciences paper reported that epitalon-activated telomerase enhanced bovine oocyte maturation and post-thawed embryo development [chen2025_bovine_oocyte]. The most recent 2025 cell-line telomerase report [shamporov2025_telomere] was published with a same-year Correction [shamporov2025_correction]. None of these constitute the kind of independent, adequately powered human clinical replication that would establish the Russian preclinical and small-clinical findings.

Epitalon / Epithalon Timeline

1980s • Bovine pineal polypeptide preparation 'epithalamin' developed and used in Russian and Ukrainian clinical research as a geroprotective agent under Russian Ministry of Health authorization (preceded the synthetic AEDG tetrapeptide); long-term follow-up subsequently summarized by Korkushko et al [korkushko2011_15year]. (2011)

1990s • Synthesis and preclinical characterization of the AEDG tetrapeptide (epitalon / epithalon) at the St [khavinson2017_aedg; araj2025_overview]. Petersburg Institute of Bioregulation and Gerontology under Vladimir Khavinson, proposed as the active-fragment synthetic analog of bovine epithalamin

2002 • Anisimov et al [anisimov2002_her2]. (Bull Exp Biol Med), Epithalon decelerates aging and suppresses breast adenocarcinoma development in HER-2/neu transgenic mice; foundational lifespan-and-tumor report in a genetically defined cancer model

2002 • Khavinson (Neuroendocrinol Lett), proposes that epitalon activates chromatin in old-age cells; framing of the 'short-peptide bioregulator' hypothesis [khavinson2002_chromatin]

2003 • Khavinson, Bondarev, and Butyugov (Bull Exp Biol Med), Epithalon peptide induces telomerase activity and telomere elongation in human somatic cells; cited as the foundational mechanistic claim [khavinson2003_telomerase]

2003 • Anisimov et al [anisimov2003_lifespan]. (Biogerontology), Epitalon affects biomarkers of aging, lifespan, and spontaneous tumor incidence in Swiss-derived SHR female mice

2003 • Djeridane et al [djeridane2003_melatonin]. (J Endocrinol Invest), Synthetic pineal tetrapeptide effects on melatonin secretion by young-rat pineal gland; one of the rare independent (French-collaborator) preclinical reports of the era

2003 • Kossoy et al [kossoy2003_colon]. (Int J Mol Med), Epitalon and colon carcinogenesis in rats: proliferative activity and apoptosis

2003 • Khavinson and Shataeva (Bull Exp Biol Med), Effect of regulatory peptides on gene transcription; mechanistic framing for short-peptide nuclear action [khavinson2003_transcription]

2004 • Korkushko et al [korkushko2004_melatonin]. (Bull Exp Biol Med), Bovine peptide preparation 'epithalamin' restores circadian melatonin rhythm in elderly subjects; small Russian/Ukrainian clinical report

2004 • Anisimov SV, Khavinson VKh, Anisimov VN (Neuroendocrinol Lett), gene expression effects of a related short peptide (Cortagen) in mouse heart; companion gene-expression work for the brain [anisimov2004_heart_genes; anisimov2004_brain_genes]

2005 • Anisimov et al [anisimov2003_carcinogenesis]. (Vopr Onkol), Effect of epitalon and melatonin on life span and spontaneous carcinogenesis in senescence-accelerated SAM mice

2006 • Korkushko et al [korkushko2006_geroprotective]. (Bull Exp Biol Med), Geroprotective effect of epithalamine (bovine pineal peptide preparation) in elderly subjects with accelerated aging; small clinical report

2007 • Anisimov et al [anisimov2007_lifespan]. (Bull Exp Biol Med), Effect of Ala-Glu-Asp-Gly peptide on life span and development of spontaneous tumors in female rats exposed to different illumination regimes

2007 • Labunets et al [labunets2007_chronic_cad]. (Bull Exp Biol Med), Effect of epithalamin on the rhythm of immune and endocrine systems in patients with chronic coronary artery disease

2008 • Khavinson, Solovyov, Shataeva (Bull Exp Biol Med), Reports melting of DNA double strand after binding to a geroprotective tetrapeptide; biochemical claim cited as evidence for direct peptide-DNA interaction [khavinson2008_dna]

2011 • Korkushko, Khavinson, Shatilo, Antonyk-Sheglova (Bull Exp Biol Med), Reports 15-year follow-up of geroprotective courses of epithalamin (bovine peptide preparation) in elderly subjects [korkushko2011_15year]

2011 • Fedoreyeva et al [fedoreyeva2011_penetration]. (Biochemistry Moscow), Penetration of short fluorescence-labeled peptides into the nucleus in HeLa cells and in vivo; mechanistic supporting evidence for proposed nuclear action

2012 • Khavinson, Linkova, Chalisova, Dudkov (Bull Exp Biol Med), Effect of short peptides on expression of signaling molecules in organotypic pineal cell culture [khavinson2012_pineal_culture]

2012 • Khavinson et al [khavinson2012_melatonin_mechanism]. (Bull Exp Biol Med), Molecular cellular mechanisms of peptide regulation of melatonin synthesis in pineal organotypic culture

2015 • Esposito et al [esposito2015_analytical]. (Drug Testing and Analysis), Identification of the small research tetrapeptide epitalon as a potential substance of abuse; one of the few independent Western analytical engagements

2017 • Khavinson et al [khavinson2017_aedg]. (Bull Exp Biol Med), Identification of peptide AEDG in the polypeptide complex of the bovine pineal gland by mass spectrometry; supports the active-fragment hypothesis linking synthetic AEDG to bovine epithalamin

2019 • Khavinson, Linkova, Tarnovskaya (Int J Immunopathol Pharmacol), Effect of short peptides on neuronal differentiation of stem cells [linkova2019_neurodifferentiation]

2020 • Ashapkin et al [ashapkin2020_senescence]. (Int J Mol Sci), AEDG peptide (epitalon) stimulates gene expression and protein synthesis during human fetal-cell senescence in vitro; one of the first independent Western groups to report on AEDG mechanism

2022 • Yang et al [yang2022_oocyte]. (Aging, Albany NY), Epitalon protects against post-ovulatory aging-related damage of mouse oocytes in vitro

2025 • Araj et al [araj2025_overview]. (Int J Mol Sci), Narrative overview of epitalon as a 'highly bioactive pineal tetrapeptide'; emphasizes dependence of evidence base on the Khavinson group's preclinical and small-clinical reports and absence of independent Western replication

2025 • Shamporov et al [shamporov2025_telomere; shamporov2025_correction]. (Biogerontology), Reports epitalon increases telomere length in human cell lines through telomerase upregulation; subsequently issued a published Correction

2025 • Pankov et al. (Stem Cell Rev Rep), In-vitro wound-healing model with epitalon; Chen et al [pankov2025_wound; chen2025_bovine_oocyte]. (Life Sci), bovine oocyte maturation and post-thawed embryo development with epitalon-activated telomerase

2026 • Bagheri et al [bagheri2026_gerontology]. (Front Aging), Review of therapeutic peptides in gerontology including epitalon; reiterates the small and largely Russian-language evidence base for AEDG

Clinical Contexts for Epitalon / Epithalon

Anti-aging / geroprotection / longevity PRECLINICAL

Preclinical only in the contemporary peer-reviewed Western sense. Russian-language clinical work used the older bovine peptide preparation 'epithalamin' (not the synthetic AEDG tetrapeptide) in small open-label studies; the synthetic AEDG tetrapeptide has not been studied in adequately powered Western clinical trials. Anti-aging claims circulating in the consumer peptide market are not supported by independent Western replication.

Russian-language preclinical work in mice has reported lifespan extension and reduction of spontaneous tumor incidence with intermittent AEDG administration in Swiss-derived SHR mice, HER-2/neu transgenic mice, and senescence-accelerated SAM mice [anisimov2003_lifespan; anisimov2002_her2; semenchenko2004_lifespan]. Russian-Ukrainian small clinical reports describe geroprotective effects of the older bovine pineal polypeptide preparation 'epithalamin' (not the synthetic tetrapeptide) in elderly subjects, including a 15-year follow-up summary [korkushko2004_melatonin; korkushko2006_geroprotective; korkushko2011_15year]. These reports are small, predominantly open-label, conducted at one or two collaborating Russian and Ukrainian centers, and have not been independently replicated outside that academic network. Anti-aging and lifespan-extension claims for the synthetic AEDG tetrapeptide are not supported by Western randomized controlled trials and are not part of any FDA-approved indication [labunets2007_chronic_cad; anisimov2007_lifespan; anisimov2003_carcinogenesis].

Telomere length and telomerase activation PRECLINICAL

Single-laboratory preclinical claim with limited independent replication. Not a clinically established outcome.

Khavinson et al. (Bull Exp Biol Med, 2003) reported induction of telomerase activity and telomere elongation by AEDG in cultured human somatic cells [khavinson2003_telomerase]; the same group reported supporting evidence of chromatin and gene-expression effects [khavinson2002_chromatin, khavinson2003_transcription, anisimov2004_brain_genes]. A 2025 cell-line report in Biogerontology re-examined the telomere effect in human cell lines [shamporov2025_telomere] and was subsequently the subject of a published Correction [shamporov2025_correction]. A 2025 Life Sciences paper reported telomerase-mediated improvement of bovine oocyte maturation and post-thawed embryo development [chen2025_bovine_oocyte]. No Western randomized human trial has demonstrated a clinically meaningful effect of epitalon on human telomere length, telomerase activity, or any clinical endpoint linked to telomere biology.

Melatonin / pineal-axis modulation PRECLINICAL

Small preclinical and Russian-language clinical signals; not an established indication.

Djeridane et al. (J Endocrinol Invest, 2003), one of the rare Russian-French collaborative reports, described effects of the AEDG tetrapeptide on melatonin secretion by young-rat pineal gland [djeridane2003_melatonin]. Russian-language clinical reports by Korkushko and colleagues described modulation of circadian melatonin rhythm in elderly subjects using the bovine 'epithalamin' preparation [korkushko2004_melatonin]. Khavinson and colleagues subsequently reported pineal-organotypic-culture and molecular-mechanism work on peptide regulation of melatonin synthesis [khavinson2012_pineal_culture, khavinson2012_melatonin_mechanism]. None of these establish a clinically validated melatonin-modulating indication for the synthetic AEDG tetrapeptide in US practice.

Off-Label Uses of Epitalon / Epithalon

Consumer 'research peptide' anti-aging market PRECLINICAL

Not a clinical use. Epitalon is widely sold online to consumers as a research peptide for anti-aging purposes, outside any regulated quality system.

Esposito et al. (Drug Testing and Analysis, 2015) identified epitalon in research-grade peptide preparations and characterized the substance in the context of analytical detection of potential substances of abuse [esposito2015_analytical]. Most circulating consumer-facing 'epitalon' or 'epithalon' material is sold under research-peptide labeling that explicitly disclaims human therapeutic use; the material is not manufactured under FDA-registered facilities, is not the subject of an FDA-reviewed identity-and-purity specification, and does not carry sterility, endotoxin, or potency assurances of a 503A-compounded sterile preparation. The Araj 2025 overview and the Bagheri 2026 review describe the gap between the consumer-marketed anti-aging narrative and the absence of independent Western clinical replication [araj2025_overview, bagheri2026_gerontology].

FDA-Approved Uses of Epitalon / Epithalon

Epitalon has no FDA-approved indication and no FDA-approved branded finished drug product in the United States. There is no NDA, ANDA, or BLA approval, no over-the-counter monograph, no FDA-approved label, no approved patient population, no approved dosing regimen, and no FDA-registered manufacturer.

Epitalon is not on the FDA 503A bulk drug substances Category 1 list. It is treated by RonanRx by analogy to other research peptides under FDA review as a Category 2-equivalent compound: not eligible for routine 503A patient-specific compounding pending FDA review [fda503a, fda_bulks_category2]. Russian and Ukrainian regulatory authorizations and pharmacopeial entries for the historical bovine 'epithalamin' polypeptide preparation, and any Russian-Federation-specific status of the synthetic AEDG tetrapeptide, are jurisdiction-specific to those countries and have no bearing on US drug status.

Compounded Epitalon / Epithalon (503A)

Physicians may submit patient-specific prescription requests for pharmacy review. For Epitalon, certain preparations may be available now when clinically appropriate, lawfully prescribed, and approved by the dispensing pharmacy. Availability is determined case by case and may depend on patient-specific documentation, ingredient status, source qualification, formulation feasibility, state requirements, and pharmacist judgment. The review starts with the evidence constraint: The evidence base for Epitalon is

limited and uneven. It includes Russian and preclinical work around pineal peptides, sleep, and cellular aging markers, but no FDA-reviewed clinical program establishes an approved US indication.

This ingredient is part of an evolving FDA review process. RonanRx is monitoring FDA's PCAC process and any subsequent agency action. FDA has scheduled Epitalon-related bulk drug substances for discussion at the 23-24 Jul 2026 Pharmacy Compounding Advisory Committee meeting. Availability may change after FDA review, PCAC discussion, final agency action, or state-board guidance. For Epitalon, RonanRx ties that monitoring to the evidence limits described above and to any patient-specific documentation submitted by the prescriber.

Valid patient-specific prescription required. Supporting clinical rationale may be requested. Compounded medications are not FDA-approved. No consumer self-ordering, no office stock, no bulk dispensing. Requests for Epitalon are reviewed before any preparation is made or released. For Epitalon, the patient-specific route matters because consumer marketing often turns thin evidence into broad longevity claims. RonanRx review keeps the request tied to a licensed prescriber, a named patient, and pharmacist judgment.

Epitalon / Epithalon Formulations and Routes

Form	Concentration	Description
Research-grade peptide (unregulated)	—	Epitalon is supplied internationally as a research-grade synthetic peptide for laboratory use. These preparations are sold outside any regulated pharmaceutical quality system, are not manufactured under FDA-registered facilities, and do not carry compendial identity, purity, sterility, endotoxin, or potency specifications. RonanRx does not source, dispense, or counsel on research-grade epitalon.
Historical bovine 'epithalamin' polypeptide preparation (Russia / Ukraine)	—	Epithalamin is a bovine-pineal polypeptide extract used in Russian and Ukrainian clinical research from the 1980s onward under Russian-Federation regulatory authorizations. It is a pharmacologically distinct preparation from the synthetic AEDG tetrapeptide and is not available in the United States. The 15-year geroprotective follow-up and most pre-2010 clinical reports used epithalamin rather than the synthetic AEDG tetrapeptide.

Routes used in published literature: intramuscular, subcutaneous, intranasal.

Epitalon / Epithalon Dosing

Route	Population	Range	Duration	Study type
Intramuscular or subcutaneous (Russian preclinical and small clinical reports)	Adult rodents and elderly human subjects (Russian-Ukrainian academic research)	Russian-language reports describe intermittent courses of microgram-to-low-milligram doses of the synthetic AEDG tetrapeptide in rodent studies and of the bovine polypeptide preparation epithalamin in small elderly-subject clinical work. No FDA-reviewed dose exists, and reported regimens are heterogeneous across study protocols.	Intermittent courses over weeks to years in long-term Russian-Ukrainian clinical follow-up of epithalamin	Russian-language preclinical and small open-label clinical reports, does not constitute an FDA-reviewed dosing regimen
Intranasal (preclinical only)	Rats (neurophysiology studies)	Intranasal AEDG infusion has been reported in rodent neurophysiology studies modulating neuronal activity in the rat neocortex; no human intranasal dosing data are available	Acute and short-term protocols	Preclinical rodent neurophysiology

There is no FDA-approved or RonanRx-supported dosing regimen for epitalon. Russian-language preclinical reports and small Russian-Ukrainian clinical reports describe intermittent microgram-to-low-milligram parenteral courses of either the synthetic AEDG tetrapeptide or the bovine epithalamin polypeptide preparation; these regimens are heterogeneous across protocols, have not been the subject of FDA pharmacology review, and have not been validated in independent Western randomized controlled trials [araj2025_overview].

RonanRx does not publish a consumer dosing schedule for Epitalon. Any request requires a valid patient-specific prescription, supporting clinical rationale, and pharmacist review. Route, strength, dosing interval, monitoring expectations, and dispensing quantity would be determined case by case from the prescriber's documentation and pharmacy feasibility review.

Epitalon / Epithalon Safety

The published human safety database for the synthetic AEDG tetrapeptide is limited to small Russian-language reports from the Korkushko and Khavinson groups in Kiev and St [23]. Petersburg. Most of these reports use the older bovine polypeptide preparation epithalamin rather than the synthetic AEDG tetrapeptide [1117]. Within these reports, the authors describe the regimens as well tolerated in elderly subjects at the doses studied, but the reports are small, predominantly open-label, conducted at one or two collaborating centers, and have not been the subject of independent safety analysis outside the Russian-Ukrainian academic network [15].

There is no FDA safety review of epitalon, no FDA-reviewed adverse-event labeling, no FDA Adverse Event Reporting System (FAERS) analysis, no published cardiovascular safety dataset, no carcinogenicity or reproductive-toxicology package submitted to a Western regulatory authority, and no independent Western pharmacovigilance literature. Russian-language preclinical work has described favorable effects on age-related and immune endpoints [82126]; these reports do not constitute a safety database in the FDA-review sense.

Material reaching US patients is sourced almost entirely from unregulated international 'research peptide' vendors. Analytical work by Esposito et al. (Drug Testing and Analysis, 2015) [27] documents epitalon in such preparations and characterizes its analytical detectability; this work does not characterize sterility, endotoxin, identity-fidelity, or potency-fidelity of grey-market preparations, which cannot be assumed in the absence of a regulated supply chain. The FDA's general framing of research peptides under 503A bulks review applies by analogy: substances not on the Category 1 list are not eligible for routine 503A patient-specific compounding pending agency review [3938].

Contraindications

Honest gap. There is no FDA-approved label for epitalon and no FDA-reviewed list of contraindications, warnings, or precautions. Because there is no FDA-approved indication and epitalon is not on the FDA 503A bulks Category 1 list, RonanRx treats epitalon as not eligible for clinical use, which functions as a categorical contraindication to RonanRx-dispensed use.

Searched: PubMed, FDA Drugs@FDA, DailyMed, FDA 503A bulk drug substances list on 2026-05-11 · terms *epitalon OR epithalon OR AEDG OR "Ala-Glu-Asp-Gly", contraindications, warnings, precautions*.

Drug interactions

Honest gap. No published clinically validated drug-drug interaction data are available for epitalon. The molecule has not been characterized in dedicated human CYP-substrate or transporter-substrate studies in the indexed peer-reviewed literature, and there is no FDA-reviewed clinical pharmacology dataset. As a

short peptide, epitalon is expected to undergo rapid proteolytic catabolism rather than CYP-mediated metabolism, but this expectation has not been confirmed by validated human studies.

Searched: PubMed, FDA Drugs@FDA, DailyMed on 2026-05-11 · terms *epitalon OR epithalon OR AEDG drug interactions, pharmacokinetic interactions, CYP*.

Adverse events

Honest gap. No FDA-reviewed adverse-event analysis exists for epitalon. Russian-language reports of the synthetic AEDG tetrapeptide and the bovine epithalamin preparation describe the regimens as well tolerated in elderly subjects at the doses studied [korkushko2006_geroprotective, korkushko2011_15year], but these are small open-label single-network reports rather than a structured pharmacovigilance database. No published FAERS analysis is available because epitalon has never been a marketed FDA-approved drug. Unregulated international 'research peptide' supply carries the additional risks typical of grey-market injectable peptides, sterility, endotoxin, identity, and potency, which cannot be characterized at population level in the absence of a regulated supply chain [esposito2015_analytical].

Searched: PubMed, FDA FAERS public dashboard on 2026-05-11 · terms *epitalon OR epithalon OR AEDG adverse events, FAERS, postmarketing, injection-site*.

Monitoring Epitalon / Epithalon Therapy

No RonanRx-specific monitoring protocol has been established for Epitalon. If a patient-specific prescription is submitted, supporting clinical rationale may be requested, and monitoring expectations would be reviewed case by case against the published evidence, route, sterile or nonsterile status, concomitant therapies, and patient risk factors.

Epitalon / Epithalon in Special Populations

Epitalon / Epithalon Evidence Quality

The evidence base for epitalon is small, geographically and institutionally concentrated, and dominated by one research group. The St. Petersburg Institute of Bioregulation and Gerontology (Vladimir Khavinson and colleagues) and its collaborators in Kiev (the Korkushko group at the D.F [korkushko2006_geroprotective; korkushko2011_15year; vinogradova2007_muscles]. Chebotarev Institute of Gerontology) account for the large majority of the primary literature, and most reports appear in Russian-language journals (Advances in Gerontology, Bulletin of Experimental Biology and Medicine, Voprosy Onkologii, Patologicheskaia Fiziologiia i Eksperimental'naia Terapiia, Fiziologiia Cheloveka) or Eastern European outlets. Independent Western preclinical engagement is limited and recent, Djeridane et

al. 2003 (French collaboration) [djeridane2003_melatonin], Ashapkin et al. 2020 (independent gene-expression replication) [ashapkin2020_senescence], Yang et al [ilina2009_antiox]. 2022 (oocyte aging) [yang2022_oocyte], Shamporov et al [anisimov2003_lifespan; labunets2003_thymocyte]. 2025 (cell-line telomerase with subsequent published Correction) [shamporov2025_telomere, shamporov2025_correction], and the Pankov 2025 [pankov2025_wound] and Chen 2025 [chen2025_bovine_oocyte] reports, and does not amount to the scale of independent replication required to establish a Russian preclinical claim in the Western evidence-based medicine framework.

Clinical evidence in humans is restricted to small open-label reports from the Korkushko-Khavinson collaboration using the bovine polypeptide preparation 'epithalamin' rather than the synthetic AEDG tetrapeptide [korkushko2004_melatonin; labunets2007_chronic_cad]. No randomized double-blind placebo-controlled Western trial of the synthetic AEDG tetrapeptide has been published in any indication, no FDA-reviewed clinical pharmacology dataset exists, no large multi-center safety study has been conducted, and no pharmacovigilance database is available because epitalon has never been a marketed FDA-approved drug.

The Araj 2025 narrative overview [araj2025_overview] and the Bagheri 2026 peptide-therapeutics review [bagheri2026_gerontology] catalog the AEDG literature and similarly emphasize this gap. Anti-aging, telomere-extension, and lifespan-extension claims for epitalon circulating in the consumer 'research peptide' market are not supported by independent Western randomized controlled trial evidence and should not be conveyed to patients as established clinical effects [khavinson2003_telomerase; linkova2012_immune]. Analytical work [esposito2015_analytical] documents the substance in unregulated research-grade supply chains. The overall evidence quality for epitalon in any clinical indication is low: a small Russian-language preclinical and clinical literature dominated by one academic network, limited and recent independent replication, and no FDA-approved or 503A-eligible US pathway.

Major Epitalon / Epithalon Clinical Studies

Study	Design	Participants	Duration	Finding
Khavinson, Bondarev, Butyugov (2003, Bull Exp Biol Med), Telomerase induction by AEDG	In vitro report on cultured human somatic cells incubated with the AEDG tetrapeptide; telomerase activity and telomere length endpoints	—	—	Reported induction of telomerase activity and telomere elongation; foundational mechanistic claim [khavinson2003_telomerase]. Has not been independently replicated using contemporary methods in primary Western academic literature.
Anisimov et al. (2003,	Long-term mouse aging study in	—	—	Reported effects on biomarkers of aging, mean lifespan, and spontaneous tumor

Study	Design	Participants	Duration	Finding
Biogerontology), Lifespan and tumor incidence in SHR mice	Swiss-derived SHR female mice with intermittent epitalon courses			incidence [anisimov2003_lifespan]. Single-group preclinical report; not independently replicated in Western academic laboratories.
Anisimov, Khavinson, Alimova, Semchenko (2002, Bull Exp Biol Med), HER-2/neu transgenic mice	Long-term mouse aging study in HER-2/neu transgenic mice with intermittent epitalon courses	—	—	Reported deceleration of aging and suppression of breast adenocarcinoma development in a genetically defined cancer-prone mouse model [anisimov2002_her2]. Russian-laboratory preclinical report; not independently replicated.
Semenchenko, Anisimov, Yashin (2004, Exp Gerontol), HER-2/neu lifespan analysis	Analytical reanalysis of stressors and antistressors influencing lifespan in HER-2/neu transgenic mice	—	—	Reported a favorable shift in lifespan distribution with intermittent peptide courses including epitalon in the HER-2/neu model. Same academic network as Anisimov 2002 [semenchenko2004_lifespan].
Anisimov et al. (2007, Bull Exp Biol Med), AEDG lifespan in female rats under different light regimes	Long-term rodent aging study in female rats exposed to different illumination regimes with intermittent AEDG courses	—	—	Reported effect of the Ala-Glu-Asp-Gly tetrapeptide on lifespan and development of spontaneous tumors in female rats [anisimov2007_lifespan]. Russian-laboratory preclinical report.
Anisimov et al. (2005, Vopr Onkol), Epitalon and melatonin in SAM mice	Russian-language Voprosy Onkologii report on senescence-accelerated mice receiving epitalon or melatonin	—	—	Reported effects on lifespan and spontaneous carcinogenesis in senescence-accelerated mice [anisimov2003_carcinogenesis]. Russian-language preclinical report.
Korkushko et al. (2011, Bull Exp Biol Med), 15-year	Long-term Russian-Ukrainian open-label follow-	—	—	Reported reduction in rapid-aging signatures over 15 years of follow-up [korkushko2011_15year]. Small single-

Study	Design	Participants	Duration	Finding
geroprotective follow-up	up of elderly subjects receiving repeated courses of the bovine pineal polypeptide preparation 'epithalamin' (not the synthetic AEDG tetrapeptide)			network open-label report; uses the bovine polypeptide preparation rather than the synthetic tetrapeptide. Not independently replicated in Western clinical research.
Korkushko et al. (2006, Bull Exp Biol Med), Geroprotective effect in elderly with accelerated aging	Small Russian-Ukrainian open-label clinical report on elderly subjects with accelerated aging treated with the bovine 'epithalamin' polypeptide preparation	—	—	Reported geroprotective signals on multiple age-related measures. Bovine polypeptide preparation rather than synthetic AEDG; small and open-label [korkushko2006_geroprotective].
Korkushko et al. (2004, Bull Exp Biol Med), Circadian melatonin in elderly with epithalamin	Small Russian-Ukrainian open-label clinical report on elderly subjects	—	—	Reported restoration of circadian rhythm of pineal melatonin secretion with the bovine 'epithalamin' polypeptide preparation [korkushko2004_melatonin]. Small and open-label.
Labunets et al. (2007, Bull Exp Biol Med), Chronic coronary disease subjects	Russian-Ukrainian report on the bovine 'epithalamin' preparation in patients with chronic coronary artery disease	—	—	Reported effects on the rhythm of immune and endocrine systems in chronic coronary disease subjects [labunets2007_chronic_cad]. Small and open-label; bovine polypeptide rather than synthetic AEDG.
Khavinson, Solovyov, Shataeva (2008, Bull Exp Biol	In vitro biophysical study of the geroprotective	—	—	Reported melting of DNA double strand after binding to the tetrapeptide; cited as biochemical evidence for direct peptide-DNA interaction in support of the gene-

Study	Design	Participants	Duration	Finding
Med), DNA double-strand melting	tetrapeptide AEDG with DNA			promoter binding hypothesis [khavinson2008_dna].
Khavinson et al. (2017, Bull Exp Biol Med), AEDG in bovine pineal complex (MS identification)	Mass-spectrometry identification of peptides in the polypeptide complex of the bovine pineal gland	—	—	Identified the AEDG tetrapeptide sequence within the bovine pineal polypeptide complex; supports the active-fragment hypothesis linking the synthetic tetrapeptide to the historical bovine 'epithalamin' preparation [khavinson2017_aedg].
Ashapkin et al. (2020, Int J Mol Sci), Gene expression in senescent fetal cells	In vitro report on human fetal cells in replicative senescence treated with AEDG	—	—	Reported stimulation of gene expression and protein synthesis during human fetal-cell senescence [ashapkin2020_senescence]. One of the first independent Western groups to engage with the AEDG mechanism in cell culture; the result has not been integrated into a confirmed mechanism-of-action consensus.
Yang et al. (2022, Aging, Albany NY), Mouse oocyte post-ovulatory aging	In vitro study of post-ovulatory aged mouse oocytes treated with epitalon	—	—	Reported protection against post-ovulatory aging-related damage in mouse oocytes in vitro; preclinical hypothesis-generating result [yang2022_oocyte].
Shamporov et al. (2025, Biogerontology), Telomere length in human cell lines (with Correction)	In vitro report on human cell lines treated with epitalon	—	—	Reported increases in telomere length through telomerase upregulation; the paper was subsequently the subject of a published Correction [shamporov2025_telomere; shamporov2025_correction]. Independent replication has not yet appeared in primary peer-reviewed Western biochemistry literature.
Esposito et al. (2015, Drug Test Anal), Analytical identification as	Analytical-chemistry case report identifying the small research tetrapeptide	—	—	Characterized epitalon as a substance of potential abuse encountered in research-grade peptide supply chains; one of the few independent Western engagements with the molecule, focused on detection

Study	Design	Participants	Duration	Finding
substance of potential abuse	epitalon in research-grade peptide preparations			rather than clinical effect [esposito2015_analytical].

Epitalon / Epithalon Pharmacokinetics & Pharmacodynamics

Pharmacokinetics

There are no validated human pharmacokinetic data for the synthetic AEDG tetrapeptide in the indexed peer-reviewed literature. The Khavinson group has reported on the penetration of fluorescence-labeled short peptides into cell nuclei in HeLa cells and in vivo [fedoreyeva2011_penetration], framed as a cellular-uptake claim rather than a clinical PK characterization. As a short peptide, epitalon is expected to undergo rapid plasma proteolytic catabolism and to have a short half-life; this expectation has not been confirmed in published human PK studies, and no validated Cmax, Tmax, AUC, half-life, clearance, volume of distribution, or bioavailability parameters by any route appear in the Western literature.

Russian-language preclinical and clinical reports describe intermittent administration over weeks to months (or, in the long-term Korkushko 2011 follow-up of the bovine epithalamin preparation, intermittent courses across years) [korkushko2011_15year]; these are dosing-protocol descriptions rather than pharmacokinetic characterizations.

Pharmacodynamics

Pharmacodynamic effects described in the Khavinson-group preclinical literature center on telomerase activation and telomere elongation in cultured human somatic cells [khavinson2003_telomerase], chromatin and gene-expression effects in aged cells [khavinson2002_chromatin, khavinson2003_transcription, anisimov2004_brain_genes], rodent lifespan and tumor-incidence effects in genetically heterogeneous and cancer-prone mouse models, modulation of melatonin synthesis in pineal organotypic culture [khavinson2012_pineal_culture, khavinson2012_melatonin_mechanism], and modulation of immune and endocrine measures in small Russian-Ukrainian clinical reports.

Adequately powered Western clinical pharmacodynamic data confirming a sustained, clinically meaningful effect on any human endpoint have not been published [labunets2007_chronic_cad; anisimov2003_lifespan; anisimov2002_her2; anisimov2007_lifespan]. The available human-subject reports are small, predominantly open-label, conducted at one or two collaborating Russian-Ukrainian centers, and use the bovine epithalamin polypeptide preparation rather than the synthetic AEDG tetrapeptide in most cases [korkushko2004_melatonin; korkushko2006_geroprotective; korkushko2011_15year; semenchenko2004_lifespan].

Comparing Epitalon / Epithalon Formulations

There is no FDA-approved comparator formulation for epitalon. The historical bovine 'epithalamin' polypeptide preparation used in Russian and Ukrainian clinical research from the 1980s onward is pharmacologically distinct from the synthetic AEDG tetrapeptide [khavinson2017_aedg, korkushko2011_15year] and is not available in the United States. Within the broader peptide-therapeutics space, epitalon has not advanced through Western phase 1, phase 2, or phase 3 clinical development of the kind completed by other peptides such as the GLP-1 receptor agonists or thymic peptides.

Epitalon / Epithalon Storage and Handling

There is no FDA-approved storage labeling for epitalon because there is no FDA-approved product. Research-grade peptide preparations are typically supplied as lyophilized powder requiring refrigerated or frozen storage prior to reconstitution per the supplier's research-use-only labeling; these are not pharmaceutical storage specifications and are not validated by FDA review. RonanRx does not store or dispense epitalon.

Epitalon / Epithalon Compounding & Operations

503A compounding

Physicians may submit patient-specific prescription requests for pharmacy review. For Epitalon, certain preparations may be available now when clinically appropriate, lawfully prescribed, and approved by the dispensing pharmacy. Availability is determined case by case and may depend on patient-specific documentation, ingredient status, source qualification, formulation feasibility, state requirements, and pharmacist judgment. The review starts with the evidence constraint: The evidence base for Epitalon is limited and uneven. It includes Russian and preclinical work around pineal peptides, sleep, and cellular aging markers, but no FDA-reviewed clinical program establishes an approved US indication.

This ingredient is part of an evolving FDA review process. RonanRx is monitoring FDA's PCAC process and any subsequent agency action. FDA has scheduled Epitalon-related bulk drug substances for discussion at the 23-24 Jul 2026 Pharmacy Compounding Advisory Committee meeting. Availability may change after FDA review, PCAC discussion, final agency action, or state-board guidance. For Epitalon, RonanRx ties that monitoring to the evidence limits described above and to any patient-specific documentation submitted by the prescriber.

Valid patient-specific prescription required. Supporting clinical rationale may be requested. Compounded medications are not FDA-approved. No consumer self-ordering, no office stock, no bulk dispensing.

Requests for Epitalon are reviewed before any preparation is made or released. For Epitalon, the patient-specific route matters because consumer marketing often turns thin evidence into broad longevity claims. RonanRx review keeps the request tied to a licensed prescriber, a named patient, and pharmacist judgment.

Pharmacist review

For Epitalon, the pharmacist review starts before any preparation is made. Valid patient-specific prescription required. Supporting clinical rationale may be requested. The pharmacist reviews ingredient status, sourcing, formulation feasibility, state requirements, patient-specific documentation, and whether dispensing is appropriate case by case.

Quality and traceability

If a Epitalon preparation is approved after pharmacy review, RonanRx applies source documentation, formulation records, lot traceability, release checks, and storage controls appropriate to the actual dosage form. Research-use vial storage practices do not substitute for pharmacy-assigned storage, beyond-use dating, sterility controls when applicable, or recallable batch records. The patient-specific framework and quality controls are documented in the cited compounding references [usp_795; usp_797].

Cold chain

If a Epitalon preparation is approved after pharmacy review, RonanRx applies source documentation, formulation records, lot traceability, release checks, and storage controls appropriate to the actual dosage form. Research-use vial storage practices do not substitute for pharmacy-assigned storage, beyond-use dating, sterility controls when applicable, or recallable batch records.

Frequently Asked Questions About Epitalon / Epithalon

Can physicians request Epitalon through RonanRx?

Physicians may submit patient-specific prescription requests for pharmacy review. Certain preparations may be available now when clinically appropriate, lawfully prescribed, and approved by the dispensing pharmacy. Availability is determined case by case. Compounded medications are not FDA-approved, and no consumer self-ordering, office stock, or bulk dispensing is offered.

What is epitalon?

Epitalon is a synthetic four-amino-acid peptide with the sequence Ala-Glu-Asp-Gly (AEDG). It was developed at the St. Petersburg Institute of Bioregulation and Gerontology by Vladimir Khavinson and colleagues as the proposed active-fragment synthetic analog of the older bovine pineal polypeptide preparation 'epithalamin' used in Russian and Ukrainian clinical research since the 1980s [khavinson2017_aedg; araj2025_overview].

Does epitalon extend lifespan or telomeres?

Russian-language preclinical reports from one academic group describe lifespan-extension and tumor-reduction signals in mouse aging models and a single in-vitro report of telomerase induction in cultured cells [khavinson2003_telomerase; korkushko2011_15year]. These claims have not been independently replicated in primary Western randomized controlled trials or contemporary biochemistry-laboratory studies at the scale required to establish them. Anti-aging and telomere-extension claims for epitalon should not be conveyed to patients as established clinical effects [anisimov2003_lifespan; araj2025_overview].

Is epitalon FDA-approved?

No. Epitalon has no FDA-approved indication or branded product. It has not been the subject of an approved NDA, ANDA, BLA, or OTC monograph in the United States. It is not on the FDA 503A bulk drug substances Category 1 list, and RonanRx classifies it by analogy to other research peptides under FDA review as not eligible for routine 503A patient-specific compounding [fda_bulks_category2; fda503a].

What about the Russian clinical reports?

The published clinical reports, almost all from the Korkushko group in Kiev in collaboration with the Khavinson group in St [korkushko2011_15year]. Petersburg, are small open-label single-network reports and most use the older bovine pineal polypeptide preparation 'epithalamin' rather than the synthetic AEDG tetrapeptide [korkushko2004_melatonin; korkushko2006_geroprotective; labunets2007_chronic_cad]. They have not been independently replicated outside the Russian-Ukrainian academic network and do not constitute the kind of randomized double-blind placebo-controlled evidence base required for US regulatory or clinical adoption.

What should clinicians do if a patient is already using epitalon?

For Epitalon, physicians may submit patient-specific prescription requests for pharmacy review. Availability is determined case by case, and supporting clinical rationale may be requested.

References

1. *[khavinson2002_chromatin]* Khavinson VKh, Lezhava TA, Monaselidze JR, Jokhadze TA, Dvalishvili NA, Bablishvili NK, Trofimova SV. *Peptide Epitalon activates chromatin at the old age*. Neuroendocrinology Letters. 2003. PMID 14647006. (accessed 2026-05-11)
2. *[khavinson2003_telomerase]* Khavinson VKh, Bondarev IE, Butyugov AA. *Epithalon peptide induces telomerase activity and telomere elongation in human somatic cells*. Bulletin of Experimental Biology and Medicine. 2003. PMID 12937682. (accessed 2026-05-11)
3. *[khavinson2003_transcription]* Khavinson VKh, Shataeva LK, Chernova AA. *Effect of regulatory peptides on gene transcription*. Bulletin of Experimental Biology and Medicine. 2003. PMID 14666197. (accessed 2026-05-11)

4. *[anisimov2002_her2]* Anisimov VN, Khavinson VKh, Alimova IN, Semchenko AV, Yashin AI. *Epithalon decelerates aging and suppresses development of breast adenocarcinomas in transgenic her-2/neu mice*. Bulletin of Experimental Biology and Medicine. 2002. PMID 12459848. (accessed 2026-05-11)
5. *[anisimov2003_lifespan]* Anisimov VN, Khavinson VKh, Popovich IG, Zabezhinski MA. *Effect of Epitalon on biomarkers of aging, life span and spontaneous tumor incidence in female Swiss-derived SHR mice*. Biogerontology. 2003. PMID 14501183. (accessed 2026-05-11)
6. *[djeridane2003_melatonin]* Djeridane Y, Khavinson VKh, Anisimov VN, Touitou Y. *Effect of a synthetic pineal tetrapeptide (Ala-Glu-Asp-Gly) on melatonin secretion by the pineal gland of young and old rats*. Journal of Endocrinological Investigation. 2003. PMID 12809170. (accessed 2026-05-11)
7. *[kossoy2003_colon]* Kossoy G, Zandbank J, Tendler E, Anisimov V, Khavinson V, Popovich I, Zabezhinski M, Zusman I, Ben-Hur H. *Epitalon and colon carcinogenesis in rats: proliferative activity and apoptosis in colon tumors and mucosa*. International Journal of Molecular Medicine. 2003. PMID 12964022. (accessed 2026-05-11)
8. *[labunets2003_thymocyte]* Labunets IF, Butenko GM, Khavinson VKh, Magdich LV, Dragunova VA, Pishel' IN, Azarskova MV. *[Regulating effect of pineal gland peptides on development of T-lymphocytes in CBA aging mice: role of microenvironment of immune system organs and neuroendocrine factors]*. Advances in Gerontology. 2003. PMID 14743608. (accessed 2026-05-11)
9. *[anisimov2004_heart_genes]* Anisimov SV, Khavinson VKh, Anisimov VN. *Elucidation of the effect of brain cortex tetrapeptide Cortagen on gene expression in mouse heart by microarray.*. Neuroendocrinology Letters. 2004. PMID 15159690. (accessed 2026-05-11)
10. *[anisimov2004_brain_genes]* Anisimov SV, Khavinson VKh, Anisimov VN. *Effect of melatonin and tetrapeptide on gene expression in mouse brain*. Bulletin of Experimental Biology and Medicine. 2004. PMID 15723138. (accessed 2026-05-11)
11. *[korkushko2004_melatonin]* Korkushko OV, Khavinson VKh, Shatilo VB, Magdich LV. *Effect of peptide preparation epithalamin on circadian rhythm of epiphyseal melatonin-producing function in elderly people*. Bulletin of Experimental Biology and Medicine. 2004. PMID 15452611. (accessed 2026-05-11)
12. *[semenchenko2004_lifespan]* Semenchenko GV, Anisimov VN, Yashin AI. *Stressors and antistressors: how do they influence life span in HER-2/neu transgenic mice?*. Experimental Gerontology. 2004. PMID 15501020. (accessed 2026-05-11)
13. *[kazakova2005_il2]* Kazakova TB, Barabanova SV, Novikova NS, Glushikhina MS, Khavinson VKh, Korneva EA. *Synthesis of IL-2 mRNA in cells of rat hypothalamic structures after injection of short peptides*. Bulletin of Experimental Biology and Medicine. 2005. PMID 16224591. (accessed 2026-05-11)
14. *[anisimov2003_carcinogenesis]* Anisimov VN, Arutiunian AV, Khavinson VKh. *[Effect of epitalon and melatonin on life span and spontaneous carcinogenesis in senescence accelerated mice (SAM)].*. Voprosy Onkologii. 2005. PMID 15909815. (accessed 2026-05-11)
15. *[korkushko2006_geroprotective]* Korkushko OV, Khavinson VKh, Shatilo VB, Antonyuk-Shcheglova IA. *Geroprotective effect of epithalamine (pineal gland peptide preparation) in elderly subjects with accelerated aging*. Bulletin of Experimental Biology and Medicine. 2006. PMID 17426848. (accessed 2026-05-11)
16. *[morozov2007_intranasal]* Morozov VG, Khavinson VKh. *[Intranasal epitalon infusion modulates neuronal activity in the rat neocortex]*. Rossiiskii Fiziologicheskii Zhurnal Imeni I.M. Sechenova. 2006. PMID 17217245. (accessed 2026-05-11)
17. *[labunets2007_chronic_cad]* Labunets IF, Butenko GM, Korkushko OV, Shatilo VB. *Effect of epithalamin on the rhythm of immune and endocrine systems functioning in patients with chronic coronary disease.*. Bulletin of Experimental Biology and Medicine. 2007. PMID 18214303. (accessed 2026-05-11)

18. *[anisimov2007_lifespan]* Anisimov VN, Khavinson VKh, Provinciali M, Alimova IN, Baturin DA, Popovich IG, Zabezhinski MA, Imyanitov EN, Mancini R, Franceschi C. *Effect of Ala-Glu-Asp-Gly peptide on life span and development of spontaneous tumors in female rats exposed to different illumination regimes.*. Bulletin of Experimental Biology and Medicine. 2007. PMID 18856211. (accessed 2026-05-11)
19. *[khavinson2008_dna]* Khavinson VKh, Solovyov AY, Shataeva LK. *Melting of DNA double strand after binding to geroprotective tetrapeptide*. Bulletin of Experimental Biology and Medicine. 2008. PMID 19526107. (accessed 2026-05-11)
20. *[vinogradova2007_muscles]* Vingradova IA, Iliukha VA, Fedorova AS, Khizhkin EA, Unzhakov AR, Khavinson VKh. *[Age-related changes of exercise capacity and some biochemical indices of rat muscles under influence of different light conditions and pineal preparations].*. Advances in Gerontology. 2007. PMID 17969589. (accessed 2026-05-11)
21. *[ilina2009_antiox]* Il'ina TN, Vinogradova IA, Iliukha VA, Khizhkin EA, Khavinson VKh. *[The influences of geroprotectors on age-related changes of antioxidant system in rats liver under different light condition].*. Advances in Gerontology. 2008. PMID 19432171. (accessed 2026-05-11)
22. *[fedoreyeva2011_penetration]* Fedoreyeva LI, Kireev II, Khavinson VKh, Vanyushin BF. *Penetration of short fluorescence-labeled peptides into the nucleus in HeLa cells and in vitro specific interaction of the peptides with deoxyribooligonucleotides and DNA*. Biochemistry (Moscow). 2011. PMID 22117547. (accessed 2026-05-11)
23. *[korkushko2011_15year]* Korkushko OV, Khavinson VKh, Shatilo VB, Antonyk-Sheglova IA. *Peptide geroprotector from the pituitary gland inhibits rapid aging of elderly people: results of 15-year follow-up*. Bulletin of Experimental Biology and Medicine. 2011. PMID 22451889. (accessed 2026-05-11)
24. *[khavinson2012_pineal_culture]* Khavinson VKh, Linkova NS, Chalisova NI, Dudkov AV. *Effect of short peptides on expression of signaling molecules in organotypic pineal cell culture*. Bulletin of Experimental Biology and Medicine. 2011. PMID 22803060. (accessed 2026-05-11)
25. *[khavinson2012_melatonin_mechanism]* Khavinson VKh, Linkova NS, Kvetnoy IM, Kvetnaia TV, Polyakova VO, Korf HW. *Molecular cellular mechanisms of peptide regulation of melatonin synthesis in pinealocyte culture*. Bulletin of Experimental Biology and Medicine. 2012. PMID 22816096. (accessed 2026-05-11)
26. *[linkova2012_immune]* Lin'kova NS, Kuznik BI, Khavinson VKh. *[Peptide Ala-Glu-Asp-Gly and interferon gamma: their role in immune response during aging]*. Advances in Gerontology. 2012. PMID 23289226. (accessed 2026-05-11)
27. *[esposito2015_analytical]* Esposito S, Deventer K, Goeman J, Van der Eycken J, Van Eenoo P. *Identification of the small research tetra peptide Epitalon, assumed to be a potential treatment for cancer, old age and Retinitis Pigmentosa in two illegal pharmaceutical preparations.*. Drug Testing and Analysis. 2015. PMID 25535022. (accessed 2026-05-11)
28. *[khavinson2017_aedg]* Khavinson VK, Kopylov AT, Vaskovsky BV, Ryzhak GA, Lin'kova NS. *Identification of Peptide AEDG in the Polypeptide Complex of the Pineal Gland*. Bulletin of Experimental Biology and Medicine. 2017. PMID 29124531. (accessed 2026-05-11)
29. *[linkova2019_neurodifferentiation]* Khavinson VK, Lin'kova NS, Tarnovskaya SI. *Effect of short peptides on neuronal differentiation of stem cells*. International Journal of Immunopathology and Pharmacology. 2019. PMID 30791821. (accessed 2026-05-11)
30. *[ashapkin2020_senescence]* Khavinson VK, Popovich IG, Linkova NS, Mironova ES, Ilina AR. *AEDG Peptide (Epitalon) Stimulates Gene Expression and Protein Synthesis during Neurogenesis: Possible Epigenetic Mechanism*. Molecules. 2020. PMID 32019204. (accessed 2026-05-11)
31. *[yang2022_oocyte]* Yang Q, Dai S, Luo X, Zhu J, Li F, Liu J, Yao G, Sun Y. *Epitalon protects against post-ovulatory aging-related damage of mouse oocytes in vitro*. Aging (Albany NY). 2022. PMID 35413689. (accessed 2026-05-11)

32. *[araj2025_overview]* Araj SK, Brzezik J, Mądra-Gackowska K, Szeleszczuk Ł. *Overview of Epitalon-Highly Bioactive Pineal Tetrapeptide with Promising Properties*. International Journal of Molecular Sciences. 2025. PMID 40141333. (accessed 2026-05-11)
33. *[shamporov2025_telomere]* Shamporov VA, Veselovsky VA, Klimina KM, Sineva ON. *Epitalon increases telomere length in human cell lines through telomerase upregulation or ALT activity*.. Biogerontology. 2025. PMID 40908429. (accessed 2026-05-11)
34. *[shamporov2025_correction]* Shamporov VA, Veselovsky VA, Klimina KM, Sineva ON. *Correction: Epitalon increases telomere length in human cell lines through telomerase upregulation or ALT activity*.. Biogerontology. 2025. PMID 41240216. (accessed 2026-05-11)
35. *[pankov2025_wound]* Pankov AA, Pyatigorskaya NV, Beloborodov VL, Selivanova IA. *The Antioxidant Tetrapeptide Epitalon Enhances Delayed Wound Healing in an in Vitro Model of Diabetic Retinopathy*.. Stem Cell Reviews and Reports. 2025. PMID 40493162. (accessed 2026-05-11)
36. *[chen2025_bovine_oocyte]* Chen Z, Huang W, Wang L, Wei J, Zhu Y. *Epitalon-activated telomerase enhance bovine oocyte maturation rate and post-thawed embryo development*.. Life Sciences. 2025. PMID 39788414. (accessed 2026-05-11)
37. *[bagheri2026_gerontology]* Bagheri H, Salari N, Aminian H, Mohammadi M. *Therapeutic peptides in gerontology: mechanisms and applications for healthy aging*. Frontiers in Aging. 2026. PMID 42021992. (accessed 2026-05-11)
38. *[fda503a]* U.S. Food and Drug Administration. *Compounding Laws and Policies — Section 503A of the Federal Food, Drug, and Cosmetic Act*. FDA Drug Compounding. 2024. https://www.fda.gov/drugs/human-drug-compounding/compounding-laws-and-policies (accessed 2026-05-11)
39. *[fda_bulks_category2]* U.S. Food and Drug Administration. *503A Bulk Drug Substances Nominated for Use in Compounding Under Section 503A — Category 2 (Significant Safety Risks)*. FDA Drug Compounding. 2024. https://www.fda.gov/drugs/human-drug-compounding/bulk-drug-substances-used-compounding-under-section-503a-fdc-act (accessed 2026-05-11)
40. *[usp_797]* United States Pharmacopeia. *USP General Chapter <797> Pharmaceutical Compounding — Sterile Preparations*. USP Compounding Compendium. 2023. https://www.usp.org/compounding/general-chapter-797 (accessed 2026-05-11)
41. *[usp_795]* United States Pharmacopeia. *USP General Chapter <795> Pharmaceutical Compounding — Nonsterile Preparations*. USP Compounding Compendium. 2023. https://www.usp.org/compounding/general-chapter-795 (accessed 2026-05-11)

How to Access Epitalon / Epithalon

Compounded Epitalon / Epithalon is dispensed under 503A on a patient-specific prescription. Depending on your role, the next step looks different.

FOR PRESCRIBING CLINICIANS

Offer this medication

A pharmacist will follow up within two business days. We'll cover state availability, supported formulations, and what integration looks like for your clinic.

ronanrx.com/request-partnership-call

PATIENT WITH A DOCTOR

Receive your prescription

If your doctor has prescribed Epitalon / Epithalon, sign up so we can prepare and ship your medication. The signup wizard collects intake and connects you to the prescribing workflow.

ronanrx.com/patients

PATIENT WITHOUT A DOCTOR

Find a partner clinic

RonanRx prescribes through partner clinics — we don't initiate prescriptions on this site. Read how the referral process works and how to find a partner clinic in your state.

ronanrx.com/find-clinic

Other compounds RonanRx makes

This monograph is one of many in the RonanRx formulary. Every compound below is prepared under 503A on a patient-specific prescription. Browse the full catalog at ronanrx.com/medications and ronanrx.com/peptides, or scan the codes at right for each index.

Medications

Peptides

MEDICATIONS (40)

Alpha-Lipoic Acid (ALA) — Antioxidant & mitochondrial
Coenzyme Q10 (CoQ10) — Antioxidant & mitochondrial
Glutathione — Antioxidant & mitochondrial
NAD+ / NMN — Antioxidant & mitochondrial
Compounded Topical Anesthetics (BLT, LET) — Dermatology
Topical Minoxidil — Dermatology
Topical Tretinoin — Dermatology
Compounded Magnesium — Energy & nutritional
Cyanocobalamin — Energy & nutritional
High-Dose Vitamin D — Energy & nutritional
Hydroxocobalamin — Energy & nutritional
Iron (Compounded) — Energy & nutritional
L-Carnitine — Energy & nutritional
Methylcobalamin (B12) — Energy & nutritional
Methylfolate — Energy & nutritional
Anastrozole — Hormone optimization
Clomiphene & Enclomiphene — Hormone optimization
DHEA — Hormone optimization
Estradiol — Hormone optimization
Estriol — Hormone optimization
Human Chorionic Gonadotropin (HCG) — Hormone optimization
Pregnenolone — Hormone optimization
Progesterone — Hormone optimization
Testosterone — Hormone optimization
Compounded Metformin — Metabolic & weight
Compounded Semaglutide — Metabolic & weight
Compounded Tirzepatide — Metabolic & weight
Lipotropic Injection (MIC, MICC) — Metabolic & weight
Low-Dose Naltrexone (LDN) — Metabolic & weight
Naltrexone-Bupropion Combination — Metabolic & weight
Topiramate — Metabolic & weight
Bremelanotide / PT-141 — Sexual health
Compounded Sildenafil — Sexual health
Compounded Tadalafil — Sexual health
Trimix Injection — Sexual health
Compounded Gabapentin — Sleep & recovery
Compounded Melatonin — Sleep & recovery
Compounded T3 (Liothyronine) — Thyroid
Compounded T3/T4 Combinations — Thyroid
Compounded T4 (Levothyroxine) — Thyroid

PEPTIDES (21)

Sermorelin — Available now

Tesamorelin — Available now

AOD-9604 — Growth-hormone axis (under FDA review)

CJC-1295 — Growth-hormone axis (under FDA review)

GHRP-2 / GHRP-6 — Growth-hormone axis (under FDA review)

Hexarelin — Growth-hormone axis (under FDA review)

Ipamorelin — Growth-hormone axis (under FDA review)

MK-677 / Ibutamoren — Growth-hormone axis (under FDA review)

5-Amino 1MQ — Metabolic & longevity (under FDA review)

Epitalon / Epithalon — Metabolic & longevity (under FDA review)

MOTS-C — Metabolic & longevity (under FDA review)

Thymosin Alpha-1 / Thymalin — Metabolic & longevity (under FDA review)

DSIP, Delta Sleep-Inducing Peptide — Neuro & cognitive (under FDA review)

Selank — Neuro & cognitive (under FDA review)

Semax — Neuro & cognitive (under FDA review)

Vasoactive Intestinal Peptide (VIP) — Neuro & cognitive (under FDA review)

BPC-157 — Tissue repair (under FDA review)

KPV — Tissue repair (under FDA review)

LL-37 — Tissue repair (under FDA review)

Pentadeca Arginate (PDA) — Tissue repair (under FDA review)

TB-500 / Thymosin Beta-4 — Tissue repair (under FDA review)