

# PE-22-28

Patient Education Guide — What It Does, Why a Physician Would Prescribe It, and What the Evidence Says

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## Important Disclaimer

This information is not medical advice and is provided only to help begin your research. All clinical and dosing decisions must be made with a licensed, experienced physician and a licensed, experienced compounding pharmacist, supported by published clinical studies. This material was compiled using Artificial Intelligence, statements from videos and websites by apparent qualified professionals, and available published research. Anyone starting a medication they have never taken before should take an extremely conservative approach. We are not affiliated with any of the doctors whose videos are referenced below.

## PE-22-28 Investigational Research Compound

**Also known as:** Mini-Spadin

**Category:** Cognitive & Neurological Support — TREK-1 Channel Blocker

**What it is.** PE-22-28 is a synthetic seven-amino-acid peptide spanning residues 22 through 28 of spadin—a naturally occurring fragment cleaved from the propeptide of sortilin. It is entirely unrelated to Pinealon despite the two being discussed together in nootropic circles and sold together in blends; we separate them here for exactly that reason.

**How it works.** The story starts with TREK-1, a two-pore-domain potassium channel expressed heavily in the hippocampus, cortex, and amygdala. Mice genetically lacking TREK-1 are resistant to depression in standard behavioral models—a finding that identified the channel as a drug target. A 2010 *PLoS Biology* paper identified spadin as a natural TREK-1 blocker with fast-onset antidepressant-like effects. PE-22-28 was engineered as a shorter, more stable, dramatically more potent version: roughly 0.12 nM IC<sub>50</sub> against TREK-1, several hundred times more potent than spadin, with activity lasting up to about 23 hours. Blocking TREK-1 increases neuronal excitability in mood-relevant regions and, in rodents, drives hippocampal neurogenesis and BDNF expression within days.

**The honest evidence picture—and the cautions.** The animal data is genuinely interesting: antidepressant-like behavior within about four days, versus the four to six weeks conventional antidepressants require. What does not exist is human data. No completed, published human efficacy trial. No validated human dose. No FDA approval. Sources framing it as a "ketamine alternative" are mechanistically wrong and clinically premature. Cautions include psychiatric instability, suicidality, and bipolar disorder—mood-active compounds can destabilize psychiatric patients quickly, and casual experimentation here is dangerous medicine. Because TREK-1 also has roles in cardiac electrophysiology and pain signaling, cardiac disease raises theoretical questions that have not been studied in humans. Pregnancy, nursing, and anyone under 18: no data at all, so no. Active psychiatric disease needs mental health care, not a research peptide.

**Published Evidence:** Mazella et al. (*PLoS Biol*, 2010) identified spadin as a sortilin-derived TREK-1 blocker producing rapid antidepressant effects in mouse models. Djillani et al. (*Front Pharmacol*, 2017) synthesized a library of shortened spadin fragments and identified PE-22-28 as the lead candidate on binding affinity, plasma stability, and behavioral effect, reporting increased neurogenesis and synaptogenesis. All of it is preclinical.

### Key Studies:

- Mazella J, et al. "Spadin, a sortilin-derived peptide, targeting rodent TREK-1 channels: a new concept in the antidepressant drug design." *PLoS Biol*. 2010;8(4):e1000355.
- Djillani A, et al. "Shortened Spadin Analogs Display Better TREK-1 Inhibition, In Vivo Stability and Antidepressant Activity." *Front Pharmacol*. 2017;8:643.

## Recommended Videos (educational, independent sources)

► **LIVV Natural** — What You Need to Know About PE-22-28 Peptide

<https://www.youtube.com/watch?v=sYjh2jIl59M>

