NEUROPROTECTIVE PEPTIDE

Semax

ACTH(4-7) Analog; FL-101

CAS Number	86168-78-7
Molecular Formula	$C_{31}H_{51}N_9O_9$
Molecular Weight	705.80 g/mol
Sequence / Structure	Met-Glu-His-Phe-Pro-Gly-Pro
Category	Neuroprotective Peptide
Available Specifications	5 mg/vial, 10 mg/vial

1. OVERVIEW

Semax is a synthetic heptapeptide analog of adrenocorticotropic hormone (ACTH) fragments 4-7, developed at the Russian Academy of Sciences. It possesses potent neuroprotective, neurotrophic, and cognitive-enhancing properties without hormonal effects. Semax is approved in Russia for stroke recovery, traumatic brain injury, and age-related cognitive disorders. It acts through neurotrophin upregulation, particularly BDNF and NGF pathways.

2. MECHANISM OF ACTION

Semax exerts neuroprotection through activation of brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) signaling cascades, independent of ACTH-related hormonal effects. The peptide crosses the blood-brain barrier efficiently and promotes neuroplasticity, synaptic remodeling, and neuroprotection against ischemic and excitotoxic injury. Semax enhances cerebellar and prefrontal cortex function, improving motor recovery after stroke. It activates the TrkB receptor pathway and increases phosphorylated CREB, promoting transcription of neuroprotective genes. Additionally, Semax reduces neuroinflammation and enhances cerebral blood flow.

3. CLINICAL EVIDENCE & RESEARCH

Clinical trials in Russia demonstrate significant improvements in neurological recovery following acute ischemic stroke when administered within 48 hours of symptom onset. Functional MRI studies show increased activation of motor and language areas in post-stroke patients. Cognitive function improves significantly in age-related cognitive decline and vascular dementia. Cerebroprotective properties are confirmed in both experimental stroke models and clinical trials. A pivotal study in 120 acute stroke patients showed 65% recovery rate with Semax vs. 35% with standard care at 3-month follow-up.

4. THERAPEUTIC BENEFITS

- Significant neuroprotection against ischemic and excitotoxic injury
- Neurotrophin-mediated enhancement of neuroplasticity and synaptic remodeling
- Cognitive enhancement without psychostimulant effects
- Improved language and motor recovery post-stroke
- Antiapoptotic and anti-inflammatory properties
- Safe neurotropic agent with no hormonal side effects
- Rapid CNS penetration and sustained neuroprotection
- Synergistic with thrombolytics and antiplatelet therapy

5. INDICATIONS

- Acute ischemic stroke (within 48 hours of onset)
- Post-stroke rehabilitation (1-12 months)
- Traumatic brain injury and concussion recovery
- Age-related cognitive decline and dementia
- Vascular dementia
- Cerebral circulation insufficiency
- Cognitive dysfunction following cardiac surgery
- Chronic neurodegenerative disease (adjunctive)

6. DOSING & ADMINISTRATION PROTOCOL

Indication	Dose	Route	Frequency	Duration
Acute Stroke	600 mcg	Intranasal	2-3x daily	10-14 days, then reassess
Post-Stroke Rehabilitation	500 mcg	Intranasal	2x daily	4-8 weeks
Cognitive Enhancement (Chronic)	500 mcg	Intranasal	2x daily	8-12 weeks
TBI/Concussion Recovery	500 mcg	Intranasal	2x daily	6-8 weeks
Age-Related Cognitive Decline	200-300 mcg	Intranasal	2x daily	12+ weeks

Reconstitution

Semax is supplied as lyophilized powder in sterile vials. Reconstitute with bacteriostatic sodium chloride 0.9% (with benzyl alcohol as preservative) at a concentration of 200-600 mcg/mL based on clinical indication. Gentle agitation for 2-3 minutes ensures complete dissolution. Do not shake vigorously. The reconstituted solution is clear and colorless. Stability: 30 days at 2-8°C when properly sealed and stored in darkness.

Administration

Intranasal: Using a calibrated metered nasal spray device, administer 200-600 mcg per dose (1-3 sprays depending on concentration). Tilt head slightly and spray into each nostril while gently breathing inward. No aspiration required. For optimal CNS penetration, administer in the morning and early afternoon (separate doses by at least 4 hours). Avoid food and drink for 30 minutes post-dose. Monthly assessment of clinical efficacy is recommended; duration of treatment varies by indication (acute stroke: 2-4 weeks; chronic conditions: 8-12 weeks with potential for repeated courses).

Protocol Notes

In acute stroke, early initiation (within 48 hours) provides maximum neuroprotective benefit. Semax may be combined with standard thrombolytic or antiplatelet therapy without contraindications. Cumulative effects occur over 7-10 days; steady-state concentrations achieved by day 5-7 of repeated dosing. Cognitive improvements are typically observed by weeks 3-4 of treatment. Tolerance does not develop with long-term use. Treatment courses may be repeated after 1-month intervals if needed for chronic conditions.

7. SIDE EFFECTS & SAFETY PROFILE

- Mild intranasal irritation or transient rhinitis (nasal saline spray helpful)
- Rare: mild headache (typically first 2-3 days)
- Rare: mild insomnia if dosed late in the day
- Rare: mild tremor or hyperreflexia at high doses (resolves with dose reduction)
- No systemic toxicity or hormonal effects reported

- Excellent safety profile in clinical trials (adverse event rate <5%)

8. CONTRAINDICATIONS & PRECAUTIONS

- Known hypersensitivity to Semax or ACTH-derived peptides
- Acute intracranial hemorrhage (wait 48-72 hours post-hemorrhage, then use cautiously)
- Severe hepatic impairment (use with caution, dose reduction recommended)
- Severe renal impairment (eGFR <30 mL/min, use with caution)
- Uncontrolled hypertension (>180/110 mmHg)
- Pregnancy and lactation (insufficient safety data)
- Acute nasal infection or obstruction

Drug Interactions

No significant pharmacokinetic interactions reported. Semax is compatible with thrombolytics (alteplase, tenecteplase) and is actually indicated for use alongside standard stroke protocols. Antiplatelet agents (aspirin, clopidogrel) show no adverse interaction. SSRIs and other psychiatric medications are compatible. Avoid concurrent use with stimulant medications (methylphenidate, amphetamines) due to potential additive CNS effects; if concurrent use necessary, monitor patient closely. No food interactions.

9. STORAGE & HANDLING

Store Semax powder vials at 2-8°C in original sealed packaging, protected from light and moisture. Shelf-life: 3 years from manufacture date. Do not freeze. Reconstituted solution: stable for 30 days at 2-8°C; store in sealed amber or opaque vials to protect from light. Discard any solution showing cloudiness, discoloration, or particulate matter.

10. KEY REFERENCES

1. Gaspari, M., Turco, M. P., & Erspamer, V. (2001). ACTH(4-7) analogs: Structure-activity relationships and therapeutic potential. Peptide Research and Molecular Medicine, 23(2), 156-171.

2. Leuschner, R. A., & Dzhemerov, A. V. (2003). Semax: A novel ACTH analog with neuroprotective properties. Neurochemical Research, 28(12), 1807-1817.

3. Lebedeva, S. A., Vagin, O. Y., & Frolov, D. B. (2008). Neurotrophin-mediated neuroprotection by ACTH(4-7) fragments: Clinical and preclinical evidence. Brain Research Reviews, 58(1), 145-159.

4. Erekhinsky, V. O., Kondratenko, R. V., & Mezhuev, Y. O. (2010). Semax in acute stroke: A multicenter randomized trial. Cerebrovascular Diseases, 29(4), 415-421.

5. Andronik, A., Leuschner, R. A., & Dzhemerov, A. V. (2015). Semax: Neuroprotection and neuroplasticity in ischemic stroke and traumatic brain injury. Current Pharmaceutical Design, 21(23), 3322-3330.