COGNITIVE LONGEVITY PROGRAM

Low-Dose Selegiline · Methylene Blue

Prescriber Reference Guide · The Medicine Shoppe, York PA

Neuroprotection · Mitochondrial Support · Dopaminergic Tone · Physician-Supervised · Cash Pay

Program Overview

The Cognitive Longevity Program combines two compounded agents — low-dose selegiline and methylene blue — to address cognitive aging, mental fatigue, and neurological resilience through complementary mechanisms. These are prescription compounds, not supplements. Dosing, monitoring, and drug interaction screening require physician oversight.

Key Clinical Advantages

- Dual-pathway approach — dopaminergic modulation (selegiline) + mitochondrial energy support (methylene blue)
- Non-controlled — no DEA scheduling, no prescribing restrictions, no prior authorization
- Favorable safety profile at low doses — distinct from standard therapeutic doses of either agent
- Compounded to precise low doses — unavailable in commercial formulations at these ranges
- Cash pay, simple pricing — no insurance processing burden

Low-Dose Selegiline — Mechanism & Rationale

Selegiline (deprenyl) is FDA-approved for Parkinson's disease at standard doses (5–10 mg/day), where it functions as an irreversible MAO-B inhibitor. At low doses (1–5 mg), it produces selective, dose-dependent MAO-B inhibition without the dietary tyramine restrictions associated with non-selective MAO inhibition at higher doses.

Mechanism of Action

MAO-B Inhibition	Selectively inhibits monoamine oxidase B, the primary enzyme responsible for dopamine catabolism. Results in reduced dopamine breakdown and elevated dopaminergic tone in striatal and prefrontal circuits.
Dopaminergic Support	Enhanced dopamine availability supports executive function, working memory, motivation, and mood. Prefrontal dopamine signaling is a well-established target in cognitive aging.
Neuroprotective Effects	Preclinical and clinical data support neuroprotective properties beyond MAO-B inhibition — including reduced oxidative stress, anti-apoptotic effects, and possible upregulation of neurotrophic factors (BDNF, GDNF).
Longevity Data	Animal studies and some human observational data suggest selegiline may extend functional lifespan via effects on dopamine metabolism and free radical scavenging. Active area of ongoing investigation.
Dose Selectivity	At ≤5 mg/day, MAO-B selectivity is maintained and dietary tyramine restrictions (required with MAO-A inhibition) are not necessary. Above 10 mg/day, selectivity is lost — this program stays within the selective range.

Methylene Blue — Mechanism & Rationale

Methylene blue (MB) is a redox-active phenothiazine dye with a long history in medicine — used at high doses for methemoglobinemia, and at low doses as a metabolic and cognitive agent. At low doses (≤2 mg/kg), it acts as an alternative electron carrier in the mitochondrial electron transport chain, with antioxidant and signaling properties distinct from its high-dose pharmacology.

Mechanism of Action

Mitochondrial Enhancement	Functions as a redox cycler, shuttling electrons directly within the mitochondrial electron transport chain — bypassing dysfunctional complexes I–III. Increases ATP production in neurons and improves cellular energy efficiency.
Antioxidant Activity	At low doses, MB scavenges reactive oxygen species (ROS) and reduces mitochondrial oxidative stress — a key driver of neuronal aging and cognitive decline.
Neuroprotection	Studied for neuroprotective effects in models of Alzheimer's disease, traumatic brain injury, and ischemia. Proposed mechanisms include tau aggregation inhibition and mitochondrial rescue.
Nitric Oxide Signaling	MB inhibits guanylate cyclase and modulates nitric oxide pathways — relevant to cerebrovascular tone and neurovascular coupling.
Treatment-Resistant Depression	Investigated as an MAOI-independent adjunct in TRD. Proposed mechanisms involve monoamine modulation and mitochondrial effects on neuroplasticity.
Dose Dependency	Low-dose MB (≤2 mg/kg) produces cognitive-enhancing and antioxidant effects via hormetic mechanisms. Higher doses paradoxically inhibit the same mitochondrial pathways. Precise dosing is essential — compounding enables this.

Rationale for Combination Therapy

Selegiline and methylene blue target cognitive aging through distinct, complementary mechanisms — upstream dopaminergic signaling and downstream mitochondrial energy production. Together they address the two principal biological substrates of cognitive decline:

Low-Dose Selegiline	Methylene Blue
Dopamine / Neurotransmitter Pathway	**Mitochondrial / Energy Pathway**
✓ MAO-B inhibition → elevated dopamine	✓ Enhanced ATP synthesis in neurons
✓ Executive function & working memory	✓ Reduced oxidative stress / ROS
✓ Motivation, drive, mood	✓ Cognitive clarity & processing speed
✓ Neuroprotective / anti-apoptotic	✓ Neuroprotective / anti-aging

Drug Interactions & Contraindications

⚠ Critical Prescribing Warnings

- Serotonergic agents — Selegiline at any dose carries risk of serotonin syndrome when combined with SSRIs, SNRIs, TCAs, tramadol, meperidine, dextromethorphan, linezolid, or other serotonergic drugs. Screen carefully; allow adequate washout when transitioning.
- Sympathomimetics — Avoid concurrent use of stimulants, ephedrine, pseudoephedrine, and high-tyramine foods at higher doses. At low doses (≤5 mg), dietary restriction is generally not required but discuss with patients.
- Methylene blue is a potent MAOI — combined with selegiline, it adds to MAO inhibition. The low doses used in this program are designed to remain below the threshold of clinically significant serotonergic risk, but the combination requires careful patient selection and monitoring.
- G6PD deficiency — Methylene blue is contraindicated in patients with glucose-6-phosphate dehydrogenase deficiency (causes hemolytic anemia at any dose).

Additional Interaction Considerations

Dopaminergic agents	Additive dopaminergic effects with levodopa, other MAO-B inhibitors (rasagiline, safinamide). Avoid concurrent use.
Antipsychotics	Dopamine receptor antagonists may blunt the intended dopaminergic benefits. Use with caution in patients on antipsychotics.
Anticholinergics	Caution with concurrent anticholinergic burden — cognitive effects may be counteracted.
MB + Serotonergics	Methylene blue inhibits MAO-A at higher doses. At doses used in this program (≤1 mg/day), risk is substantially lower but not absent. Avoid in patients on serotonergic medications unless risk-benefit has been carefully assessed.
G6PD Screening	Obtain G6PD status prior to initiating methylene blue. Defer initiation until deficiency is excluded.

Dosing & Administration

Selegiline — Suggested Starting Protocol

Starting Dose	1 mg orally once daily (morning preferred — avoid evening to minimize insomnia risk)
Titration	Increase to 2–3 mg/day after 2–4 weeks if well tolerated; maximum 5 mg/day within the selective MAO-B range
Maintenance	2–5 mg/day; individualize based on response and tolerability
Administration	Morning dosing preferred — selegiline and its metabolites (amphetamine derivatives) may cause insomnia if dosed in the evening
Reassessment	Evaluate at 6–8 weeks; most patients report meaningful benefit within 4–12 weeks

Methylene Blue — Suggested Starting Protocol

Starting Dose	0.5 mg/kg orally once daily — compounded oral solution or capsules; titrate based on response and tolerability
Target Dose Range	0.5–1 mg/kg/day; maximum 2 mg/kg/day (above this, hormetic benefit reverses)
Administration	May be taken with food; solution can be diluted in juice to mask color/taste. Note: may cause transient blue-green discoloration of urine — counsel patients proactively.
Formulation Note	Pharmaceutical-grade methylene blue required — industrial/dye-grade preparations are NOT appropriate for human use. Compounded by The Medicine Shoppe from USP-grade raw material.
Reassessment	Evaluate cognitive and energy outcomes at 6–8 weeks; dosing can be optimized based on response

Monitoring Recommendations

Baseline	G6PD level (methylene blue contraindicated if deficient); medication reconciliation for serotonergic drugs; CBC if clinically indicated
Follow-Up (6–8 Weeks)	Assess cognitive and energy outcomes; review tolerability; screen for insomnia, GI symptoms, or mood changes
Ongoing	Annual medication review; reassess indication and drug interactions with any new prescription
Serotonin Syndrome Vigilance	Educate patients on warning signs: agitation, tremor, diaphoresis, hyperthermia, clonus. Discontinue immediately and seek emergency care if suspected.
Urine Discoloration	Blue-green urine is expected and harmless with methylene blue — document patient counseling to prevent unnecessary alarm

Formulation & Dispensing

Dosage Form	Oral capsules and/or oral solution — compounded at The Medicine Shoppe from pharmaceutical-grade USP materials
Selegiline Strengths	1 mg, 2 mg, 3 mg, 5 mg capsules — custom strengths available on request
Methylene Blue	Custom mg/mL oral solution or capsules; dose calculated per patient weight
Excipients	Compounded without unnecessary dyes or fillers; microcrystalline cellulose used as needed; MB solution in purified water with flavoring available
Quantity	30-day supply standard; 90-day available
Pricing	Cash pay — contact pharmacy for current program pricing
BUD	Per USP compounding standards; labeled on each preparation

Ordering & Contact Information

All preparations require a valid prescription. Patients fill directly at our pharmacy. No prior authorization — straightforward cash pay pricing.

How to Order

- By phone — call (717) 846-0500; ask for the compounding pharmacist; have patient name, DOB, compound(s), dose, and quantity ready
- By fax — send prescription to (717) 845-8767; specify compound, dose, quantity, and any titration instructions
- E-prescribe — select 'Compound' as medication type; include compound name, dose, and strength in the Sig/Comments field

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