Frontier Health and Wellness

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Memantine for Autism Spectrum Disorder: Understanding the Rationale and Science

Purpose of This Handout

- This handout is designed for parents who want to understand the scientific and clinical reasoning behind our use of memantine (brand: Namenda) in select children with autism spectrum disorder (ASD).
- While memantine is FDA-approved for Alzheimer's disease in adults, it is being studied for a specific subgroup of autistic children who may have a neurochemical imbalance involving glutamate, the brain's primary excitatory neurotransmitter.
- This document explains how this idea developed, who may benefit, how we identify likely responders, and what limitations exist in our ability to measure this process directly.

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1. Why Memantine Is Considered for Some Children With Autism

- Autism is a spectrum, not a single biology.
- In some children, the brain's communication systems are dominated by excessive excitatory signaling, particularly involving glutamate.
- When glutamate (a neurotransmitter) activity is too high, neurons remain in a state of overactivation — producing symptoms such as sensory hypersensitivity, chronic tension, and difficulty calming down after stimulation.

Memantine (also known under the brand name Namenda) acts as a low-affinity NMDA receptor antagonist, meaning it dampens excessive glutamate signaling without shutting down normal brain activity.

In individuals whose symptoms arise from an "overactive" neural network, this mechanism can restore better balance in glutamate neuronal systems. The result may be improved self-regulation, greater sensory tolerance, and better engagement with others.

However, if a child's brain chemistry is not dominated by excessive excitatory activity — for instance, if they struggle more with low motivation or social withdrawal rather than overarousal — memantine is less likely to be helpful.

What Memantine Is Not

Memantine is not a cure for autism. It is not a replacement for behavioral, educational, or social interventions that remain essential for development.

It should not be expected to change the child's core identity or erase the traits that make them who they are.

It is not a fast-acting medication. Research protocols continue to track improvements over weeks and months.

It will not produce an extraordinary transformation. When it helps, improvement is usually gradual — often seen as reduced irritability, better tolerance for stimulation, or an improved ability to participate in daily interactions.

Memantine is not FDA-approved for autism; its use for this purpose is considered off-label and by some definitions experimental. The decision to use it is based on published scientific evidence and clinical reasoning rather than formal regulatory approval.

> **LIMITATION:** Studies using advanced brain imaging showed 80% of children with a specific glutamate pattern improved on memantine. Clinics don't have access to that imaging. Alternate screening tools are expected to be less accurate, making an 80% response rate unlikely in a clinical setting.

Finally, memantine is not suitable or helpful for every child with autism. Current research suggests it may be most beneficial in those with a very specific profile.

Memantine: The Potential
Memantine may help some children on the autism spectrum who struggle with high emotional reactivity, sensory overload, or difficulty calming once upset.

Parents who see benefit most often describe changes such as:

- Fewer or less intense meltdowns and faster recovery after distress
- Greater tolerance for noise, touch, or transitions
- Better ability to think before reacting
- Improved social interactions
- A general sense of being calmer, more focused, or more comfortable in their surroundings

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2. The "High-Glutamate" Subtype: Who They Are and Why They Matter

Recent neuroimaging research has identified a subset of autistic children whose brains show elevated glutamate levels in the pregenual anterior cingulate cortex (pgACC) — a region near the front of the brain involved in emotion regulation, attention shifting, and social processing.

This subgroup often presents clinically with:

- **Sensory hyperreactivity** (over-response to sound, light, or touch)
- **Autonomic overarousal** (heart rate elevation, sweating, or startle reactions)
- **Emotional volatility** (quick to anger or distress, slow to calm)
- **Paradoxical medication sensitivity** (stimulants or SSRIs increase anxiety or agitation)

Children without this profile — those who are quieter, less reactive, or socially disengaged without physiological overarousal — generally did not show measurable improvement to this medication in studies.

3. How Researchers Identified the Glutamate Pattern

The best available research tool for detecting this type of glutamate dysregulation is proton magnetic resonance spectroscopy (^{1}H-MRS), a specialized form of MRI that measures brain metabolites.

In multiple clinical trials, children with higher pgACC glutamate peaks before treatment were the ones most likely to improve on memantine. Those without that elevation were poor responders.

Unfortunately, this form of screening requires specialized MRI hardware, expert interpretation, and academic research protocols. It is not clinically available in Alaska or in most community settings.

This creates a gap between what research can identify and what clinicians can measure in practice.

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4. Bridging That Gap: The Glutamatergic Profile Screener for Autism (GPS-A)

Because we are unable to use the ^{1}H-MRS imaging protocol to isolate those with this type of glutamate dysregulation, our team developed a structured screening tool specifically for this purpose — the Glutamatergic Profile Screener for Autism (GPS-A) — to estimate which children are most likely to fit this "high-glutamate" profile.

The GPS-A is a 20-question parent questionnaire developed at Frontier Health and Wellness to help screen in children who may have a pattern of sensory and emotional overactivation often seen in the subgroup of autistic children most likely to benefit from memantine.

Developing the GPS-A

The GPS-A was designed by synthesizing:

- Findings from published neuroimaging and neurochemical research linking glutamate to overarousal and sensory reactivity, and
- Peer-reviewed research that identify which autistic signs and symptoms are most consistently associated with this type of glutamate dysregulation.
- Patterns repeatedly observed in clinical practice among children who respond to interventions that modulate excitatory balance.

The GPS-A is not a diagnostic test, nor does it measure brain chemistry directly. Instead, it organizes parent observations across several domains—sensory reactivity, emotional regulation, attention, and response to stimulation or medication—to *estimate* whether a child's behaviors fit the profile associated with glutamate overactivity.

Higher total scores suggest a stronger match with this "high-glutamate" behavioral pattern. The results guide discussion with your FHW provider and help determine whether a time-limited memantine trial might be appropriate.

Limitations

The GPS-A is not a diagnostic or biochemical test. It does not measure this process directly.

The GPS-A provides a proxy behavioral profile that parallels what ^{1}H-MRS studies have identified as glutamate-related overactivation.

Although imperfect, it represents our best, evidence-informed tool to approximate this subgroup in our clinical setting.

Because it is research-informed and not research-vetted it will certainly screen-out some children that may respond to memantine and will screen-in some that will not respond to memantine.

As with all screening tools, interpretation is individualized and integrated with clinical judgment.

Why FHW Needed To Develop The GPS-A

The relationship between glutamate overactivity and memantine response in autism is a very new scientific finding. When such connections are first discovered, it typically takes 5–10 years of additional research before reliable clinical tools are created, validated, and widely available.

At this early stage, the only definitive way to identify the subgroup that benefits most is through ^{1}H-MRS imaging — a technology unavailable in most clinical settings.

Rather than wait a decade for formal tools to reach clinical practice, we chose to bridge that gap now by creating an evidence-informed screening tool based on both research data and observed clinical patterns.

We recognize that this approach is imperfect — meaning we will sometimes identify children who do not have this glutamate pattern (false positives) and may occasionally miss some who do (false negatives).

However, by using the GPS-A, we can proactively identify and support more children today who may respond to this mechanism of treatment — children who might otherwise wait years to reap its benefits.

AT A GLANCE: Because this research is still new, the GPS-A helps us use the best current evidence to guide treatment now, rather than waiting years for formal screening methods to become available.

In other words, this tool reflects a clinically responsible middle ground: we acknowledge the limits of current science, act on the best evidence available, and accept a measured degree of uncertainty in exchange for the opportunity to reduce avoidable suffering and social impairment in children who may benefit now.

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5. Known Safety Profile

Memantine has a long safety history in adults and has been studied in children with autism, ADHD, and other developmental conditions. Long term safety data in children is not known.

In pediatric studies, the most common side effects were mild and included:

- Headache
- Irritability
- Gastrointestinal upset
- Insomnia or sleepiness
- Dizziness

Severe adverse reactions were rare (<2%), and discontinuation due to side effects was uncommon.

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6. Long-Term Use: What We Know — and Don't Know

Studies in children with autism show that most side effects from memantine are mild and short-lived.

However, nearly all available studies have followed participants for six months or less, so we do not yet have reliable data on long-term safety or how the medication might influence brain development over time.

In adults, memantine has been used for longer periods and is generally viewed as one of the safer medications affecting brain chemistry. Still, research suggests that long-term use may slowly change how the brain regulates glutamate activity.

> After about a year, some adults report reduced motivation, mild cognitive dulling, or emotional "flattening." These changes are not established to be from memantine, are uncommon and usually resolve after the medication is reduced or stopped, but they highlight why careful re-evaluation is important over time.

These motivational, cognitive and emotional responses are based on case series, clinical observation, and patient self-report, not controlled trial data. Such effects are not well-documented in the Alzheimer's literature but occasionally mentioned in off-label psychiatric use (e.g., depression, OCD, or ADHD augmentation studies).

Because the glutamate system plays a key role in brain development, particularly in learning, attention, and sensory balance, there is reason to be cautious about prolonged use during childhood. Animal studies suggest that high levels of NMDA receptor blockade during development can temporarily alter these pathways, though no human data confirm this and the degree of blockade in such studies far exceeds that produced by memantine.

For these reasons, our clinic approaches memantine as a time-limited and closely monitored trial, not a long-term or indefinite treatment. Each decision is individualized and guided by observed benefit, side effects, and functional progress.

Re-Evaluation and Discontinuation Protocol

We conduct structured reviews of treatment effectiveness at start, during each titration dosing change, 8 weeks after the titration is complete and monthly thereafter. If the child continues to show meaningful improvement, treatment may continue with careful monitoring. If benefits plateau at any point, side effects appear, or functional gains are no longer evident, we recommend tapering and discontinuing the medication.

Even when improvements during the first year are clear, we recommend a serious discussion about pausing or stopping after 12 months, since pediatric data remain limited and adult case-studies imply possible cumulative or adaptive effects over time.

Any decision to continue beyond one year should be deliberate, data-informed, and supported by ongoing clinical observation to ensure continued benefit and safety.

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7. Cost and Access

Because memantine is not FDA-approved for autism, insurance coverage is not expected.

Cost: As of lare 2025, GoodRx was listing 60 tablets of the 10 mg strength for under $20, making it comparable to co-pays insurance rates for many non-preferred medications.

Access (Bernie's Pharmacy): The off-label nature of memantine for autism in children introduces the risk of pharmacy-level interruptions. For this reason, participating families within this protocol will be requested to have their memantine prescriptions filled at Bernie's Pharmacy. Their independent structure eliminates corporate barriers, and using one pharmacy ensures a uniform manufacturer supply, reducing confounding factors from excipients or manufacturer-specific impurities.

Bernie's Pharmacy Contact Information:

- Address: 4100 Lake Otis Pkwy, Suite 200, Anchorage, AK 99508
- Phone: (907) 562–2138 | Fax: (907) 561–0752
- Hours: Mon–Fri 9:00–6:00 | Sat 10:00–2:00 | Sun closed
- RxLocal App: Available for iPhone/Android

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8. Final Word

Memantine's mechanism — reducing excessive glutamate activity — aligns with the neurobiological pattern seen in a specific subset of children with autism. These children have higher levels of hyperreactivity and physiological overarousal.

- **What we know:** Children with ASD and evidence of glutamatergic hyperexcitability are the most likely to benefit from memantine, but even for them, the benefits are not guaranteed.
- **What we cannot yet do:** Measure glutamate directly without research-grade MRI spectroscopy.
- **What we can do:** Use the GPS-A tool and individualized assessment to identify likely candidates and track results objectively.
- **Our guiding principle:** Use enough to help, and long enough to know—but not longer than necessary to maintain progress.

This structured, evidence-informed method transforms the medication approach from “trial and error” into guided clinical decision-making grounded in neurobiology.

The larger goal is to reduce the neurological noise that interferes with comfort, learning, and social connection — giving each child a better platform for development.