Medications & Behavior in LGS

LGS Foundation Family Resource

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What to watch for and what to do, all in one place. Use this as a guide for conversations with your neurologist, not a reason to stop any medication. Seizures themselves also affect behavior.

Watch closely | **Worth monitoring** | **Generally stable** | **In trials**

Perampanel

Watch closely — highest concern

The only seizure drug with an FDA warning label specifically for behavioral effects.

What families may notice

Anger, aggression, or personality changes, even in people with no prior history. Most people tolerate it fine, but when behavioral changes happen they can be severe. This is why the FDA requires a specific warning on the label.

What to do

Start at the lowest dose and increase very slowly. Keep a daily behavior log for the first 6 weeks. Before starting, ask your neurologist: 'What signs should we watch for, and when do we call you?'

Levetiracetam

Watch closely

Most commonly noticed behavioral side effect among LGS families is 'Levetiracetam rage.'

What families may notice

Irritability, mood swings, and aggressive outbursts can occur. More common in children. Doesn't happen to everyone and often improves over time.

What to do

Log behavior before starting. If worsening occurs, tell your neurologist. A switch to brivaracetam or adding vitamin B6 (pyridoxine) may help. Ask your doctor. Never stop suddenly.

Clobazam

Monitor

Some LGS children had increased agitation in the clinical trial, most often during dose increases, and most events resolved on their own or with a dose adjustment.

What families may notice

Agitation and aggression most often happen during dose increases. Can look like sudden mood changes or increased defiance.

What to do

Watch most closely in the first weeks after a dose increase. Never stop clobazam abruptly, always taper slowly with your neurologist.

Zonisamide

Monitor

Can cause irritability and mood changes alongside cognitive slowing.

What families may notice

Irritability and mood instability alongside a 'foggy' feeling. Less common than with Levitiracetam or Permpanel.

What to do

Monitor mood and behavior at each dose change. Discuss dose adjustment if irritability or cognitive slowing appears.

Brivaracetam

Monitor — milder than Levetiracetam

Most families who switched from Levetiracetam saw behavioral improvement.

What families may notice

Similar to levetiracetam, but causes behavioral side effects noticeably less often. The risk is meaningfully lower.

What to do

If levetiracetam caused behavioral problems, ask about switching to brivaracetam. Still monitor for irritability, but expect a better profile.

Topiramate

Monitor — mainly cognitive

'Topiramate fog' affects about people at higher doses. Mood changes are less common.

What families may notice

Word-finding difficulty and mental slowing are the main concerns. Mood changes can occur. Aggression is rarely a concern, though some people notice increased irritability.

What to do

Titrate slowly. Cognitive effects are much worse when the dose is raised quickly. A lower dose often preserves seizure benefit with far fewer effects.

Valproate

Generally stable

Most families don't notice behavioral changes. First-line for LGS in 2025 expert guidelines.

What families may notice

One of the most behaviorally neutral options available. Well-established across LGS literature.

What to do

Regular liver and blood tests are needed. A strong first choice when behavioral stability is already a priority. Manage drug interactions carefully.

Lamotrigine

Generally stable

Behaviorally neutral to slightly positive. Low sedation.

What families may notice

Some evidence of mild mood-stabilizing properties. Low sedation can help with alertness and engagement during the day.

What to do

Must be titrated very slowly. Raising the dose too quickly risks a skin rash that can become serious. Slow titration is the key protection. Good when you want low behavioral and cognitive burden alongside seizure control.

Rufinamide

Generally stable

Families generally don't report behavioral worsening. Good for drop seizures.

What families may notice

Behavioral stability was specifically confirmed in the 2025 comprehensive LGS review. Particularly effective for drop seizures.

What to do

Take with food. Strong choice when drop seizures are the main concern and behavioral stability needs to be preserved.

Cannabidiol

Stable — possible mood benefit

Some families report their child seems calmer or more engaged.

What families may notice

Fenfluramine

Stable — arousal benefit

Works on the serotonin system. Some families notice improved calm and emotional regulation.

What families may notice

Bexicaserin

Promising — in trials

Most-watched trial in LGS for quality-of-life outcomes. Not yet available.

What families may notice

Works through a completely different pathway than other seizure medicines. Behavioral stability confirmed in the 2025 LGS review. **What to do** Requires regular liver blood tests, which is especially important alongside valproate. Sedation can increase when combined with clobazam.	Serotonin regulates mood and emotional responses. Behavioral stability confirmed in the 2025 LGS review. **What to do** Requires a heart scan before starting and every 6 months. Only available through a special enrollment program your neurologist handles (REMS).	Early signals suggest it may help both seizures and mood, alertness, and emotional regulation via the serotonin system. Phase 3 results not yet published. **What to do** Not yet available.

Never stop without calling first Stopping suddenly can trigger dangerous seizure clusters. Always taper with your neurologist.	**Log before you start** Track behavior 1-2 weeks before any change, then 4-6 weeks after. This is a reliable way to know if the drug caused it.	**Seizures affect behavior, too** A drug with some risk may still be right if it reduces seizures, because seizures also worsen behavior.	**Ask before you start** 'If behavior gets worse, what's our plan?' Answer this before starting.

Medical disclaimer: For educational purposes only. Never stop or adjust a seizure medication without guidance from your neurologist. Sources: *Samanta et al., Epilepsy & Behavior 2025;164:110272* | *Steinhoff et al., Epilepsy & Behavior 2021;118:107939* | *Auvin et al., Epilepsia Open 2025;10:85-106* | *Kit Date: June 2026*

Doctor Visit Checklist

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Use this before any appointment where a medication change might be discussed. Bring it with you and check off each question as you cover it. You don't need to ask all of them. Find the section that fits where you are right now.

Before you start a new medication

☐	**What behavioral side effects should we watch for with this drug specifically?**	*Different drugs have different risks. Knowing what to look for helps you catch it early.*
☐	**How common are behavioral side effects with this drug in LGS patients?**	*Sets realistic expectations without needing to read the full research.*
☐	**If behavior gets worse after we start this, what is our plan and when should we call you?**	*Having this answer in advance turns a potential crisis into a manageable next step.*
☐	**Should I keep a behavior log before we start? What should I track?**	*A baseline makes it much easier to tell whether the drug caused any change.*

If you've noticed behavioral changes on a current medication

☐	**Could this behavior change be from the medication, or is it likely something else?**	*Seizures, sleep disruption, and developmental changes can look like medication side effects.*
☐	**Is there a dose adjustment that might reduce the behavioral effect while keeping seizure control?**	*Many side effects are dose-dependent — a smaller dose often makes a big difference.*
☐	**If we want to switch, what is the safest way to do that — and what would we switch to?**	*Switching always needs a careful plan. Brivaracetam is one option your neurologist may consider if Keppra is the problem.*
☐	**Is the seizure reduction we're getting worth the behavioral cost?**	*Your neurologist can help weigh this tradeoff with you honestly.*

When behavior is already a concern, how do we choose what to try next?

☐	**Given the behavioral challenges we're dealing with, which LGS medications have the best behavioral profile?**	*Valproate, lamotrigine, rufinamide, cannabidiol, and fenfluramine are generally more stable.*
☐	**Is there any medication on our current list you'd consider reducing because of behavioral risk?**	*Simplifying can sometimes improve both behavior and seizures.*
☐	**Are there clinical trials open right now that track behavioral outcomes?**	*Bexicaserin (Phase 3) and others are specifically tracking quality-of-life outcomes.*

For the newly diagnosed

☐	**What is our first-line plan, and what will we try if it doesn't work after 3 months?**	*Having a roadmap reduces anxiety and sets realistic expectations.*
☐	**Are there medications you would NOT recommend given our child's behavioral profile?**	*Some neurologists proactively avoid higher-risk drugs in children with known behavioral challenges.*
☐	**What non-medication options should we think about alongside medications?**	*Diet, VNS, and surgery matter from the start — not just after multiple drugs have failed.*

My notes before the appointment:	

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