



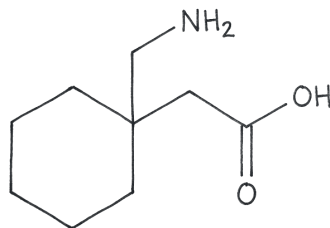
CLINICAL MONOGRAPH · SLEEP & RECOVERY

# Compounded Gabapentin

## *Gabapentin in liquid or alternative excipient preparations*

Gabapentin is a long-used prescription medicine for nerve pain and certain kinds of seizures. The brand-name versions are Neurontin (approved in 1993), Gralise (a once-daily form for shingles-related nerve pain), and Horizant (a slow-release form for restless legs syndrome). Despite its name, gabapentin does not act on GABA receptors, it works by quieting overactive nerves through a different protein on calcium channels [gee1996].

RonanRx compounds gabapentin only when a prescriber documents that the manufactured product cannot meet a patient-specific need. Common reasons include children or adults with swallowing difficulty who need a liquid at a strength not commercially available, patients with a documented sensitivity to dye or another excipient in the brand, or clinicians prescribing a topical cream or gel for a small area of localized nerve pain, a use that is off-label and not commercially manufactured [fda\_label\_neurontin; fda\_label\_gralise; fda\_label\_horizant]. Compounded preparations are not FDA-approved and are not substitutes for the manufactured products [fda\_essentially\_a\_copy].



EVIDENCE POSTURE

FDA APPROVED

WELL STUDIED

REVIEWED 2026-05-11





State-licensed  
503A



Pharmacist  
reviewed



Doctor  
led



Cold-chain  
ready



Patient choice  
preserved



# Contents

Click any section to jump there. Page numbers update on render.

Why personalized	6
Quick facts	6
How this differs from research-use-only	8
What it is	8
How it works	8
Biological role	9
Detailed mechanism	9
Research history	10
Timeline	11
Clinical contexts studied	13
Off-label uses	17
FDA-approved use	17
Compounded form (503A)	18
Formulations and routes	19
Dosing	20
Safety	21
Monitoring	23
Special populations	24
Evidence quality	24
Major studies	24
Pharmacology (PK/PD)	30
Comparative formulations	31
Storage	31
Compounding & operations	32
FAQ	33



References	35
How to access	38



## FOR CLINICIANS

Gabapentin is a GABA structural analog approved as Neurontin (1993) for adjunctive partial-onset seizures in adults and pediatric patients  $\geq 3$  years and for postherpetic neuralgia (PHN) in adults, as Gralise (2011) for once-daily PHN, and as gabapentin enacarbil (Horizant, 2011) for moderate-to-severe restless legs syndrome (RLS) and PHN [fda\_label\_horizant]. Despite the structural similarity to GABA, gabapentin is not a GABA receptor agonist; it is a high-affinity ligand of the  $\alpha 2\delta$ -1 auxiliary subunit of voltage-gated calcium channels [gee1996], reducing presynaptic calcium influx and excitatory neurotransmitter release in nociceptive and epileptogenic circuits [sills2006].

Pivotal evidence: postherpetic neuralgia [rowbotham1998], painful diabetic peripheral neuropathy [backonja1998], adjunctive partial seizures (gabapentin monotherapy study group, Chadwick 1998 Neurology [chadwick1998]; SANAD partial-epilepsy unblinded RCT, Marson 2007 Lancet [marson2007]), RLS (gabapentin enacarbil phase 3 and PK/PD program [hayes2012, lal2013, lal2011]), generalized anxiety/social phobia/panic (Pande social phobia 1999 [pande1999\_socphobia], Pande panic 2000 [pande2000\_panic]), fibromyalgia [arnold2007], hot flashes in breast cancer [pandya2005], and alcohol use disorder [mason2014] [rice2001]. The Cochrane 2017 review of gabapentin for chronic neuropathic pain in adults [wiffen2017] is the standard meta-analytic synthesis.

Safety: respiratory depression risk with concomitant CNS depressants (opioids, benzodiazepines) and in older adults with renal impairment prompted an FDA Drug Safety Communication in December 2019 [fda\_safety\_2019]; population-based Ontario data [gomes2017] documented elevated opioid-related death risk with concurrent gabapentin [fda\_label\_gralise; fda\_essentially\_a\_copy]. Misuse signal characterized systematically by Smith and colleagues [smith2016] with subsequent pharmacology and pharmacy-policy commentary [evoy2021, covvey2023]. The 503A role at RonanRx is custom oral suspensions for pediatric or dysphagia patients at strengths outside Neurontin 250 mg/5 mL, allergen-free or dye-free capsules, and topical 6, 10% creams or gels for localized off-label neuropathic pain [knezevic2017, boardman2008], only on a documented patient-specific clinical need not met by Neurontin, Gralise, or Horizant [fda\_label\_neurontin].



## ☞ Why Personalized Compounded Gabapentin

Neurontin's labeled dose schedule (300 mg day one, 600 mg day two, 900 mg day three, titrate to 1800, 3600 mg/day in three divided doses) was calibrated for an average adult with adequate kidney function and no specific sensitivity to the dye, sweetener, or flavoring in the commercial 250 mg/5 mL oral solution. That schedule does not account for a six-year-old who needs precise mg/kg dosing in a volume a child will actually swallow, an older adult with a creatinine clearance of 35 where the label demands a dose cut but the commercial strengths skip past the step you want, a patient with a documented reaction to FD&C yellow or to sorbitol in the brand solution, or a clinician trying to treat a small patch of post-surgical neuropathic pain on the foot where systemic gabapentin's sedation and gait risk are not worth it.

Compounding closes those gaps one at a time. A 50 mg/mL dye-free, sucrose-free oral suspension lets a pediatric prescriber dose by weight without a sweetener the child reacts to. A 50 mg or 200 mg custom capsule gives the older adult with renal impairment a titration step the commercial 100/300/400 mg strengths do not provide. A 6% or 10% topical gel keeps the molecule on the skin over the painful area instead of putting a sedating dose through the whole central nervous system, a route the manufacturer does not make. In every oral case the molecule is the same gabapentin the FDA reviewed in 1993; what changes is the strength, the excipient profile, and the route, fitted to one patient on one prescription.

This is what pharmacy looked like before mass manufacturing. A doctor wrote the prescription for a named patient, and a pharmacist prepared it for that patient. Modern 503A oversight, state licensure, batch documentation, pharmacist review of concomitant CNS depressants, keeps the older arrangement honest.

## ⚡ Quick Facts About Compounded Gabapentin

**Category:** Anticonvulsant / gabapentinoid,  $\alpha 2\delta$ -1 ligand of voltage-gated calcium channels (not a GABA receptor agonist despite the name)

**Active ingredient:** Gabapentin, a  $\gamma$ -aminobutyric acid (GABA) structural analog that binds the  $\alpha 2\delta$ -1 auxiliary subunit of voltage-gated calcium channels in the central nervous system

**FDA-approved branded forms:** Neurontin (immediate-release capsule, tablet, oral solution; approved 1993), Gralise (gastric-retentive once-daily tablet for postherpetic neuralgia; approved 2011), and Horizant



(gabapentin enacarbil extended-release prodrug for restless legs syndrome and postherpetic neuralgia; approved 2011)

**Route:** Oral (capsule, tablet, solution) for manufactured products; compounded preparations include patient-specific oral suspensions, custom-strength capsules, and topical creams/gels for off-label localized pain

**Evidence posture:** FDA-approved indications (postherpetic neuralgia, adjunctive partial seizures, RLS for the enacarbil prodrug) supported by pivotal randomized trials; large additional well-studied evidence base for off-label diabetic peripheral neuropathy, fibromyalgia, hot flashes, and alcohol use disorder

**FDA-approval status:** Manufactured Neurontin, Gralise, and Horizant are FDA-approved. Compounded gabapentin preparations are not FDA-approved.

**Compounded under:** 503A, patient-specific prescription only, where the manufactured FDA-approved product is not clinically appropriate (excipient sensitivity, dose individualization outside commercially available strengths, dysphagia requiring liquid not in stock, or topical use not commercially available)

**Important compounding caution:** Neurontin oral solution (250 mg/5 mL), capsules (100, 300, 400 mg), and tablets (600, 800 mg) are commercially available alongside Gralise and Horizant. Compounding of an essentially-a-copy preparation is restricted under FDA section 503A guidance; RonanRx compounds gabapentin only when the prescriber documents a patient-specific clinical reason that the manufactured product cannot meet, not for preference or price.

**Safety signal:** Risk of respiratory depression with concomitant opioids, benzodiazepines, or in older adults with renal impairment; FDA 2019 drug safety communication required new warnings. Misuse and diversion are documented at population scale.

**SPECIALS: PATIENT-SPECIFIC PRESCRIPTION ONLY**

Compounded Gabapentin described in this monograph is a 503A compounded preparation. Every dose is made on a prescription, for a named patient, by a licensed pharmacist. It is not a stocked, mass-manufactured product.

- **Made to order, not off a shelf.** No batch sits in a warehouse waiting for buyers. Your prescription triggers the prep.
- **Named-patient label.** The bottle carries one patient's name. The batch records carry one prescription.
- **Dose, strength, and route chosen for the patient.** A prescriber decides what gets compounded, not a manufacturer who set the strength for a trial population.
- **Licensed pharmacist on the hook.** A real person, with a license that can be pulled, signs off on every prep. State inspectors check the facility.
- **Compounded drugs are not FDA-approved.** They should not be evaluated using branded-drug trial data alone. Availability varies by state and prescribed medication.



## ✓ How This Differs from a Research-Use-Only Website

A research-use-only website ships a vial from a warehouse. There is no prescription, no pharmacist, no facility inspection, and no way to recall the product if something is wrong with it. If the vial is mislabeled, contaminated, or under-potent, there is nobody whose license is at stake.

A 503A compounding pharmacy is the other thing. The doctor writes the prescription. A licensed pharmacist, whose name is on the label, prepares the medicine in a facility the state inspects. If something goes wrong, there is a person and a license on the hook, and a documented chain of custody on every lot. That accountability is what makes it safe.

## 📖 What is Compounded Gabapentin?

Gabapentin (1-(aminomethyl)cyclohexaneacetic acid) is a synthetic structural analog of  $\gamma$ -aminobutyric acid (GABA), originally developed at Parke-Davis as an anticonvulsant. Despite the GABA-mimetic design and trade name (Neurontin), gabapentin does not bind GABA-A or GABA-B receptors at therapeutic concentrations and is not converted to GABA in vivo at clinically meaningful rates. The molecule is a small zwitterionic amino acid taken up by the L-type amino acid transporter in the gut and across the blood-brain barrier, which produces saturable, dose-dependent oral absorption.

The FDA-approved manufactured products are Neurontin (immediate-release capsule 100, 300, 400 mg; tablet 600, 800 mg; oral solution 250 mg/5 mL; approved 1993), Gralise (gastric-retentive once-daily extended-release tablet 300, 600 mg; approved 2011 for postherpetic neuralgia), and Horizant (gabapentin enacarbil, an extended-release prodrug that is converted to gabapentin during intestinal absorption; tablet 300, 600 mg; approved 2011 for moderate-to-severe primary restless legs syndrome and 2012 expansion for postherpetic neuralgia) [fda\_label\_horizant]. The three products are not interchangeable: gastric-retentive Gralise and the gabapentin enacarbil prodrug Horizant differ from immediate-release Neurontin in bioavailability and dose-proportionality, and labels for each carry distinct titration schedules [fda\_label\_gralise].

Compounded gabapentin is prepared on patient-specific prescription as (1) oral suspensions or solutions at custom strengths and excipient profiles when Neurontin 250 mg/5 mL is not clinically appropriate, (2) custom-strength capsules to support an individualized titration step or to exclude a sensitizing excipient, or (3) topical 6, 10% creams or gels for off-label localized neuropathic pain, a route and indication that is not commercially manufactured [fda\_label\_neurontin; gee1996; sills2006].

## ⚙️ How Compounded Gabapentin Works

Gabapentin binds with high affinity to the  $\alpha 2\delta$ -1 auxiliary subunit of voltage-gated calcium channels in the central nervous system [gee1996]. The  $\alpha 2\delta$ -1 subunit modulates the trafficking and gating of high-voltage-



activated (Ca<sub>v</sub>) calcium channels in presynaptic terminals. Gabapentin binding reduces calcium influx during depolarization, decreasing the release of excitatory neurotransmitters, glutamate, substance P, calcitonin gene-related peptide, and noradrenaline, particularly in sensitized nociceptive pathways and in epileptogenic circuits with upregulated  $\alpha 2\delta$ -1 expression [sills2006].

Importantly, gabapentin is not a GABA receptor agonist. The naming reflects the molecule's GABA structural homology rather than its mechanism. Selective  $\alpha 2\delta$ -1 ligand activity also distinguishes gabapentin and pregabalin from older anticonvulsants that act through sodium-channel blockade or direct GABA-A receptor potentiation. The clinical phenotype, anticonvulsant, antineuralgic, and anxiolytic effects with comparatively mild sedation and an absence of GABA-A withdrawal-style discontinuation, is consistent with the  $\alpha 2\delta$ -1 mechanism.

## ☉ Biological Role of Compounded Gabapentin

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Gabapentin is not an endogenous molecule. It is a synthetic small molecule developed to mimic GABA structurally and cross the blood-brain barrier, with a mechanism of action that turned out to be unrelated to GABAergic signaling. Its biological footprint is restricted to high-affinity binding at  $\alpha 2\delta$ -1 (and to a lesser extent  $\alpha 2\delta$ -2) auxiliary calcium channel subunits, with downstream reduction of presynaptic excitatory neurotransmission in pathologically sensitized or hyperactive neurons [gee1996, sills2006].

## ⚠ Detailed Mechanism of Compounded Gabapentin

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$\alpha 2\delta$ -1 is one of four  $\alpha 2\delta$  subunit isoforms ( $\alpha 2\delta$ -1 through  $\alpha 2\delta$ -4) that associate with the pore-forming  $\alpha 1$  subunit of voltage-gated calcium channels. The  $\alpha 2\delta$ -1 subunit is upregulated in dorsal root ganglion neurons and dorsal horn after peripheral nerve injury and in seizure foci, providing a mechanistic substrate for gabapentin's selectivity in pathologic states. The radioligand binding studies by Gee et al. (1996) demonstrated saturable, high-affinity gabapentin binding to a porcine brain membrane fraction that was subsequently identified as the  $\alpha 2\delta$ -1 subunit [gee1996], and subsequent work mapped the binding site to a specific RRR/RKR motif in the von Willebrand factor type A domain of  $\alpha 2\delta$ -1 [fda\_label\_horizant].

Downstream, reduced calcium influx at the presynaptic terminal decreases neurotransmitter vesicle fusion in a use-dependent manner. The mechanism predicts a state-dependent profile, therapeutic in sensitized or pathologically active circuits, comparatively quiet in normal physiology, that matches gabapentin's clinical safety profile of low intrinsic neurologic toxicity outside the dose-dependent sedation common to centrally active medications [fda\_label\_horizant]. The mechanism review by Sills (2006) synthesized the  $\alpha 2\delta$  literature and remains the standard mechanistic reference [sills2006].

Pharmacokinetically, oral gabapentin absorption is mediated by the saturable L-type amino acid transporter in the proximal small intestine. Bioavailability decreases with increasing dose (60% at 300 mg, ~35% at 1600 mg per dose), a non-linearity that motivates divided dosing (typically three times daily for



immediate-release Neurontin). Gabapentin is not metabolized, is not bound to plasma proteins, and is eliminated unchanged in the urine with a half-life of 5, 7 hours and clearance proportional to creatinine clearance. Dose adjustment is required for renal impairment per the Neurontin and Gralise labels [fda\_label\_neurontin, fda\_label\_gralise]. Gabapentin enacarbil (Horizant) is an actively transported prodrug absorbed across the entire small intestine and colon via MCT-1 and SMVT transporters; it is enzymatically cleaved to gabapentin during absorption, producing extended-release gabapentin exposure with linear, dose-proportional pharmacokinetics that overcome the saturable absorption of the parent drug [lal2011, lal2013, cundy2010] [fda\_label\_horizant].

## 🕒 Compounded Gabapentin Research History

Gabapentin was developed at Parke-Davis (later Warner-Lambert, now Pfizer) in the late 1970s and 1980s as a lipophilic GABA analog intended to cross the blood-brain barrier and to act as an anticonvulsant. The molecule was approved by FDA as Neurontin in December 1993 as adjunctive therapy for partial-onset seizures in adults, on the basis of the pivotal 1993 placebo-controlled studies (including the International Gabapentin Monotherapy Study Group; Chadwick 1998 Neurology [chadwick1998] subsequently extended efficacy data to monotherapy) [fda\_label\_neurontin]. The labeled indication was expanded to postherpetic neuralgia (PHN) in 2002 following the Rowbotham 1998 JAMA pivotal RCT [rowbotham1998], with Rice 2001 [rice2001] providing a second independent RCT, and the Backonja 1998 JAMA painful diabetic neuropathy RCT [backonja1998] establishing a parallel evidence base for off-label neuropathic pain indications.

Identification of the mechanism followed the clinical approval: Gee and colleagues (1996, J Biol Chem) [gee1996] characterized gabapentin as a high-affinity ligand of an auxiliary subunit of voltage-gated calcium channels that was later identified as  $\alpha 2\delta$ -1; the Sills 2006 mechanism review [sills2006] integrated the subsequent  $\alpha 2\delta$  literature [cundy2010]. The SANAD partial-epilepsy unblinded RCT [marson2007] placed gabapentin among the standard antiepileptic drugs for partial seizures alongside carbamazepine, lamotrigine, oxcarbazepine, and topiramate, with lamotrigine ranking favorably overall [fda\_label\_neurontin].

Off-label use accumulated through the 2000s and 2010s for generalized anxiety and social phobia [pande1999\_socphobia, pande2000\_panic], fibromyalgia [arnold2007], hot flashes in breast cancer survivors [pandya2005], and alcohol use disorder [mason2014]. Perioperative gabapentin/pregabalin as adjuncts to multimodal analgesia was systematically reviewed by Tiippana and colleagues (2007) [tiippana2007]. The 2017 Cochrane review (Wiffen and colleagues) [wiffen2017] is the standard meta-analytic synthesis for chronic neuropathic pain, reporting that gabapentin 1800, 3600 mg/day produces 50% pain reduction in approximately 30, 40% of patients with postherpetic neuralgia or painful diabetic peripheral neuropathy versus 10, 20% with placebo [lal2013]. Anticonvulsants (including gabapentin) for low back pain were demonstrated to be ineffective in a 2018 systematic review and meta-analysis



[enke2018], paralleled by the Mathieson 2017 NEJM pregabalin sciatica RCT [mathieson2017] showing no benefit of the related gabapentinoid for sciatica [fda\_label\_neurontin].

Gralise (gastric-retentive once-daily gabapentin) was approved in January 2011 for postherpetic neuralgia [fda\_label\_gralise]; gabapentin enacarbil (Horizant) was approved in April 2011 for moderate-to-severe primary restless legs syndrome with a 2012 expansion to PHN, on the basis of phase 1, 3 PK/PD and efficacy studies [fda\_label\_horizant] [hayes2012]. Misuse and diversion of gabapentin and gabapentinoids was systematically characterized by Smith and colleagues (2016, Addiction) [smith2016] with practitioner commentary by Dunlop (2016) [dunlop2016], population-scale opioid-mortality data by Gomes and colleagues (Ontario, 2017) [gomes2017], pharmacology review by Evoy and colleagues (2021) [evoy2021], and pharmacist/prescriber survey by Covvey and colleagues (2023) [covvey2023]. Goodman and Brett (2019, JAMA Intern Med) published a clinical overview of off-label gabapentinoid use, and FDA issued a Drug Safety Communication in December 2019 [fda\_safety\_2019] adding warnings for respiratory depression with concomitant CNS depressants [goodman2019]. Topical compounded gabapentin for localized neuropathic pain has been reported in case series and reviews [boardman2008, knezevic2017] [lal2011].

## 📅 Compounded Gabapentin Timeline

- 1993 • FDA approves gabapentin as Neurontin (Parke-Davis) for adjunctive therapy of partial-onset seizures in adults [fda\_label\_neurontin]

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- 1996 • Gee et al [gee1996]. characterize gabapentin as a high-affinity ligand of the  $\alpha 2\delta$  subunit of voltage-gated calcium channels in J Biol Chem, mechanistic foundation for the  $\alpha 2\delta$ -1 hypothesis

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- 1998 • Backonja et al. (JAMA) report the pivotal RCT of gabapentin for painful diabetic peripheral neuropathy; Rowbotham et al [backonja1998; rowbotham1998]. (JAMA) report the pivotal RCT of gabapentin for postherpetic neuralgia

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- 1998 • Chadwick et al [chadwick1998]. (Neurology) report the International Gabapentin Monotherapy Study Group 945-77 trial in newly diagnosed partial seizures

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- 1999 • Pande et al [pande1999\_socphobia]. (J Clin Psychopharmacol), placebo-controlled trial of gabapentin for social phobia (social anxiety disorder)

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- 2000 • Pande et al [pande2000\_panic]. (J Clin Psychopharmacol), placebo-controlled trial of gabapentin for panic disorder

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- 2001 • Rice et al [rice2001]. (Pain), second independent RCT of gabapentin for postherpetic neuralgia at 1800 mg and 2400 mg/day

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- 2002 • FDA expands Neurontin labeling to include postherpetic neuralgia in adults [fda\_label\_neurontin]



- 2005** • Pandya et al [pandya2005]. (Lancet), gabapentin for hot flashes in 420 women with breast cancer; dose-dependent reduction at 900 mg/day vs placebo
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- 2006** • Sills (Curr Opin Pharmacol) reviews the  $\alpha 2\delta$  mechanism of action of gabapentin and pregabalin [sills2006]
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- 2007** • Arnold et al. (Arthritis Rheum), gabapentin RCT in fibromyalgia; Tiippana et al [arnold2007]. (Anesth Analg) systematic review of perioperative gabapentin/pregabalin; Marson et al [tiippana2007; marson2007]. (Lancet) SANAD unblinded RCT of carbamazepine, gabapentin, lamotrigine, oxcarbazepine, and topiramate for partial epilepsy
- 
- 2008** • Boardman et al [boardman2008]. (Obstet Gynecol), topical gabapentin for localized and generalized vulvodynia case series
- 
- 2010** • Cundy et al [cundy2010]. (Int J Clin Pharmacol Ther) characterize food effect on gabapentin enacarbil pharmacokinetics, supports the dose-proportional absorption profile of the prodrug
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- 2011** • FDA approves Gralise (gastric-retentive once-daily gabapentin) for postherpetic neuralgia; FDA approves Horizant (gabapentin enacarbil prodrug) for moderate-to-severe primary restless legs syndrome [fda\_label\_gralise; fda\_label\_horizant]
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- 2011** • Lal et al [lal2011]. (Int J Clin Pharmacol Ther), phase 1 single-dose <sup>14</sup>C-radiolabeled disposition study of gabapentin enacarbil
- 
- 2012** • Hayes et al [hayes2012; fda\_label\_horizant]. (Ann Pharmacother) review gabapentin enacarbil for restless legs syndrome; FDA expands Horizant indication to postherpetic neuralgia
- 
- 2013** • Lal et al [lal2013]. (J Clin Pharmacol), population PK/PD of gabapentin after gabapentin enacarbil administration
- 
- 2014** • Mason et al [mason2014]. (JAMA Intern Med), gabapentin 1800 mg/day for alcohol use disorder; dose-dependent reduction in heavy drinking and craving
- 
- 2016** • Smith et al [smith2016; dunlop2016]. (Addiction), systematic review of gabapentin misuse, abuse, and diversion; Dunlop commentary follows in the same issue
- 
- 2017** • Wiffen et al. (Cochrane Database Syst Rev), updated meta-analysis of gabapentin for chronic neuropathic pain in adults; Gomes et al [wiffen2017; knezevic2017]. (PLoS Med), Ontario population-based nested case-control of gabapentin + opioids and opioid-related death; Knezevic et al [gomes2017]. (Pain Manag) review compounded topical analgesics including gabapentin
- 
- 2017** • Mathieson et al [mathieson2017]. (NEJM), Trial of Pregabalin for Acute and Chronic Sciatica reports no benefit, paralleling subsequent low-back-pain evidence
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- 2018 • Enke et al [enke2018]. (CMAJ), systematic review and meta-analysis of anticonvulsants (including gabapentin) for low back pain and lumbar radicular pain: no clinically meaningful benefit

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- 2019 • Goodman and Brett (JAMA Intern Med), clinical overview of off-label use of gabapentinoid drugs; FDA Drug Safety Communication (December 19, 2019) adds warnings for respiratory depression with concomitant CNS depressants or in older adults with compromised respiratory function [goodman2019; fda\_safety\_2019]

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- 2021 • Evoy et al [evoy2021]. (J Clin Pharmacol), review of gabapentinoid pharmacology in the context of emerging misuse liability

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- 2023 • Covvey et al [covvey2023]. (Res Social Adm Pharm), pharmacist, prescriber, and drug policy expert opinions on gabapentinoid misuse

## Clinical Contexts for Compounded Gabapentin

### Adjunctive therapy for partial-onset seizures (adults and pediatric ≥3 years)

FDA APPROVED

*FDA-approved indication for Neurontin.*

Gabapentin (Neurontin) is FDA-approved as adjunctive therapy for partial-onset seizures with or without secondary generalization in adults and pediatric patients ≥3 years [fda\_label\_neurontin]. The International Gabapentin Monotherapy Study Group 945-77 trial [chadwick1998] established monotherapy efficacy in newly diagnosed partial seizures, and the SANAD unblinded RCT [marson2007] placed gabapentin among standard partial-epilepsy options alongside carbamazepine, lamotrigine, oxcarbazepine, and topiramate, with lamotrigine ranking favorably on the overall outcome composite.

**Branded product:** Neurontin (gabapentin, Pfizer)



**Postherpetic neuralgia (PHN) in adults** FDA APPROVED

*FDA-approved indication for Neurontin, Gralise (once-daily gastric-retentive), and Horizant (gabapentin enacarbil).*

Three FDA-approved manufactured products carry a PHN indication: Neurontin (titrated to 1800, 3600 mg/day in three divided doses), Gralise (titrated to 1800 mg once daily with the evening meal), and Horizant (gabapentin enacarbil 600 mg twice daily) [fda\_label\_neurontin; fda\_label\_gralise; fda\_label\_horizant]. The pivotal evidence is Rowbotham 1998 JAMA [rowbotham1998] reporting a 33% reduction in average daily pain score with gabapentin 3600 mg/day vs 7.7% with placebo at 8 weeks, replicated by Rice 2001 Pain [rice2001] at 1800 mg/day and 2400 mg/day. The 2017 Cochrane meta-analysis [wiffen2017] reports that approximately 30, 40% of patients with PHN or painful diabetic peripheral neuropathy achieve 50% pain reduction on gabapentin 1800, 3600 mg/day vs 10, 20% with placebo.

**Branded product:** Neurontin, Gralise, Horizant

**Moderate-to-severe primary restless legs syndrome (RLS) in adults** FDA APPROVED

*FDA-approved indication for Horizant (gabapentin enacarbil).*

Gabapentin enacarbil (Horizant) is FDA-approved for moderate-to-severe primary RLS in adults at a maintenance dose of 600 mg once daily, taken at approximately 5 pm [fda\_label\_horizant]. The phase 1 disposition study [lal2011] and population PK/PD analysis [lal2013] supported the once-daily dosing, and the Hayes 2012 review [hayes2012] consolidated efficacy and safety. The food-effect study [cundy2010] characterizes the high-fat-meal sensitivity of the prodrug. Immediate-release gabapentin (Neurontin) is also used off-label for RLS but is not FDA-approved for this indication.

**Branded product:** Horizant (gabapentin enacarbil, Arbor Pharmaceuticals)

**Painful diabetic peripheral neuropathy** WELL STUDIED

*Off-label for gabapentin but supported by pivotal randomized evidence and standard meta-analytic synthesis.*

Backonja 1998 JAMA [backonja1998] randomized 165 adults with painful diabetic peripheral neuropathy to gabapentin titrated to 3600 mg/day or placebo for 8 weeks and reported a mean daily pain score reduction of 2.5 vs 1.4 on the 11-point numerical rating scale. The Wiffen 2017 Cochrane review [wiffen2017] places painful diabetic peripheral neuropathy in the same efficacy band as postherpetic neuralgia for gabapentin. Note that gabapentin does not have an FDA indication for painful diabetic peripheral neuropathy; pregabalin (Lyrica) and duloxetine do.



**Generalized anxiety, social anxiety disorder, and panic disorder** WELL STUDIED

*Off-label; supported by placebo-controlled trials but not FDA-approved.*

Pande and colleagues reported placebo-controlled trials of gabapentin for social phobia (1999) [pande1999\_socphobia] and panic disorder (2000) [pande2000\_panic] in the Journal of Clinical Psychopharmacology, demonstrating dose-dependent reduction in symptom scores. Gabapentin is not FDA-approved for any anxiety disorder; pregabalin carries a generalized anxiety disorder indication in Europe but not in the United States.

**Alcohol use disorder** WELL STUDIED

*Off-label; supported by a randomized clinical trial in JAMA Internal Medicine.*

Mason and colleagues (2014, JAMA Internal Medicine) [mason2014] randomized 150 adults with alcohol dependence to gabapentin 900 mg/day, gabapentin 1800 mg/day, or placebo for 12 weeks and reported a dose-dependent increase in abstinence and no-heavy-drinking days, with the 1800 mg/day arm achieving complete abstinence in 17% (vs 4% on placebo, NNT 8) and no heavy drinking in 45% (vs 23% placebo, NNT 5). Gabapentin is not FDA-approved for alcohol use disorder; naltrexone, acamprosate, and disulfiram are.

**Hot flashes (vasomotor symptoms) in breast cancer survivors** WELL STUDIED

*Off-label; supported by a Lancet randomized trial.*

Pandya and colleagues (2005, Lancet) [pandya2005] randomized 420 women with breast cancer and ≥2 hot flashes/day to gabapentin 300 mg/day, gabapentin 900 mg/day, or placebo for 8 weeks. The 900 mg/day arm reduced hot-flash severity score by 46% vs 15% with placebo. The 300 mg/day arm was not significantly different from placebo. Gabapentin is not FDA-approved for vasomotor symptoms.

**Fibromyalgia** WELL STUDIED

*Off-label; supported by a phase 2 randomized trial.*

Arnold and colleagues (2007, Arthritis & Rheumatism) [arnold2007] randomized 150 adults with fibromyalgia to gabapentin titrated to 1200, 2400 mg/day or placebo for 12 weeks and reported a 51% reduction in the Brief Pain Inventory average pain severity score with gabapentin vs 31% with placebo. Gabapentin is not FDA-approved for fibromyalgia; pregabalin, duloxetine, and milnacipran carry the indication.



**Chronic neuropathic pain (mixed etiologies)** WELL STUDIED

*Off-label for non-PHN indications; standard meta-analytic synthesis is the 2017 Cochrane review.*

The Wiffen 2017 Cochrane review of gabapentin for chronic neuropathic pain in adults [wiffen2017] pooled 37 studies (>5,900 participants) and reported moderate-quality evidence that gabapentin at 1800, 3600 mg/day produces 50% or greater pain reduction in approximately 30, 40% of patients with postherpetic neuralgia or painful diabetic peripheral neuropathy versus 10, 20% with placebo (NNT approximately 6, 8). Evidence in other neuropathic pain conditions is limited.

**Perioperative multimodal analgesia** WELL STUDIED

*Off-label; mixed evidence with safety signal of post-operative sedation and respiratory depression in opioid-naïve patients.*

Tiippana and colleagues (2007, Anesthesia & Analgesia) [tiippana2007] systematically reviewed perioperative gabapentin and pregabalin and reported modest opioid-sparing effects with increased sedation. Subsequent FDA labeling and 2019 safety communication [fda\_safety\_2019] caution about respiratory depression when gabapentinoids are combined with opioids, including in the perioperative period.

**Localized neuropathic pain, topical 6, 10% compounded cream or gel** EMERGING

*Off-label and not commercially available; small case series and topical-analgesic reviews; evidence remains limited.*

Boardman and colleagues (2008, Obstet Gynecol) [boardman2008] reported a case series of topical 2, 6% gabapentin for localized and generalized vulvodynia, with symptomatic improvement in the majority of patients. The Knezevic 2017 review of compounded topical analgesics [knezevic2017] consolidated case-series evidence for topical gabapentin alone or combined with ketamine, amitriptyline, lidocaine, or baclofen in localized neuropathic pain. The evidence base is small, single-arm or open-label, and the route is not commercially manufactured; topical compounded gabapentin remains a tier 2, 3 off-label option for localized peripheral neuropathic pain when systemic therapy is poorly tolerated or contraindicated.



## Ⓞ Off-Label Uses of Compounded Gabapentin

### Low back pain and lumbar radicular pain (sciatica) WELL STUDIED

*Off-label; randomized evidence does not support clinically meaningful benefit.*

Enke and colleagues (2018, CMAJ) [enke2018] systematically reviewed nine RCTs (859 participants) of anticonvulsants for low back pain and lumbar radicular pain and concluded that gabapentin and pregabalin do not produce clinically meaningful benefit and increase adverse events. Mathieson and colleagues (2017, NEJM) [mathieson2017] randomized 209 adults with sciatica to pregabalin or placebo and found no benefit at 8 or 52 weeks. Gabapentinoids should not be used routinely for low back pain or sciatica.

## ☑ FDA-Approved Uses of Compounded Gabapentin

Brand	Indication	Year	Route
Neurontin	Adjunctive therapy for partial-onset seizures in adults and pediatric patients ≥3 years; postherpetic neuralgia in adults	1993	Oral capsule (100, 300, 400 mg), tablet (600, 800 mg), and oral solution (250 mg/5 mL)
Gralise	Postherpetic neuralgia in adults, once-daily gastric-retentive extended-release tablet	2011	Oral tablet (300, 600 mg), titrated to 1800 mg once daily with the evening meal
Horizant	Moderate-to-severe primary restless legs syndrome in adults (2011); postherpetic neuralgia in adults (2012)	2011	Oral extended-release tablet of the gabapentin enacarbil prodrug (300, 600 mg)

Three FDA-approved manufactured gabapentin products are commercially available in the United States: Neurontin (Pfizer; approved December 30, 1993), Gralise (Almatica/Assertio; approved January 28, 2011), and Horizant (gabapentin enacarbil, Arbor Pharmaceuticals; approved April 6, 2011, with a postherpetic neuralgia expansion in 2012). The three products are not interchangeable: Gralise is a gastric-retentive once-daily formulation that requires administration with the evening meal, and Horizant is a prodrug (gabapentin enacarbil) that is absorbed across the entire small intestine and colon and converted to gabapentin during absorption, producing dose-proportional pharmacokinetics that immediate-release Neurontin does not [fda\_label\_gralise; fda\_label\_horizant].

Generic immediate-release gabapentin (capsule, tablet, and oral solution at 250 mg/5 mL) has been widely available since the early 2000s; AB-rated generics for Gralise and Horizant are also available [fda\_label\_neurontin]. Compounded gabapentin is not FDA-approved and is restricted under section 503A to patient-specific clinical needs that the manufactured products cannot meet [fda\_essentially\_a\_copy].



## ⚠ Compounded Compounded Gabapentin (503A)

Compounded gabapentin is dispensed under 503A only when the prescribing clinician documents a patient-specific clinical need that the manufactured Neurontin, Gralise, or Horizant products cannot meet [fda\_label\_gralise; fda\_label\_horizant]. Because immediate-release gabapentin is commercially available as Neurontin oral solution (250 mg/5 mL), capsules at 100/300/400 mg, and tablets at 600/800 mg, the threshold for compounding an essentially-a-copy oral preparation is high and the prescriber's clinical reason must be specific [fda\_essentially\_a\_copy].

Documented compounding indications at RonanRx fall into three primary categories. First, pediatric or adult dysphagia oral suspensions at custom strengths or excipient profiles when the commercial 250 mg/5 mL oral solution is not appropriate, for example, when the patient requires a strength outside the commercial concentration to support precise mg/kg dosing or to limit volume in a fluid-restricted patient, or when the patient has a documented sensitivity to a sweetener, preservative, dye, or flavoring in the commercial solution. Second, custom-strength solid oral preparations to support an individualized titration step (for example, 50 mg or 200 mg capsules not commercially available) or to exclude a sensitizing excipient, these are restricted under the FDA essentially-a-copy guidance and require explicit prescriber documentation. Third, topical 6, 10% gabapentin creams or gels, sometimes combined with other agents per prescriber direction, for off-label localized peripheral neuropathic pain (post-amputation neuroma, postsurgical neuropathic pain in a localized distribution, vulvodynia [boardman2008], or other small-area neuropathic conditions); the topical route is not commercially manufactured and is therefore not subject to the essentially-a-copy restriction [knezevic2017] [fda\_label\_gralise].

Compounded preparations are not bioequivalent to the manufactured products. Compounded oral suspensions and capsules should be assumed to follow the saturable, dose-dependent absorption profile of immediate-release gabapentin, with bioavailability falling from approximately 60% at 300 mg to ~35% at 1600 mg per dose [fda\_label\_neurontin]. Topical 6, 10% gabapentin preparations have not been characterized for systemic absorption in formal pharmacokinetic studies, and clinicians should not assume the systemic-route safety profile transfers; per-patient assessment of localized response is the primary endpoint, and the pharmacist's batch documentation supports traceability of strength, excipient, and beyond-use date [fda\_label\_gralise].

Misuse and diversion of gabapentin are documented at population scale [smith2016, evoy2021, covvey2023] and combination with opioids is associated with increased risk of opioid-related death [gomes2017]. FDA's December 2019 Drug Safety Communication [fda\_safety\_2019] added warnings for serious breathing problems with concomitant CNS depressants, in older adults, and in patients with compromised respiratory function. RonanRx pharmacist review explicitly evaluates concomitant medication risk before dispensing compounded gabapentin [fda\_label\_gralise].



## ⌘ Compounded Gabapentin Formulations and Routes

Form	Concentration	Description
Compounded oral suspension or solution	Custom, typically 50 mg/mL or 100 mg/mL, with patient-specific excipient profile (no dye, no sucrose, no specified flavoring, etc.)	Patient-specific oral liquid prepared under USP <795> standards for nonsterile compounding when the commercial Neurontin oral solution (250 mg/5 mL) is not clinically appropriate. Container closure, excipient profile, beyond-use date, and stability basis are documented per batch.
Compounded custom-strength capsule	Custom, typical patient-specific strengths between 25 mg and 250 mg for individualized titration steps not commercially available	Patient-specific solid oral preparation when the commercial 100, 300, 400, 600, or 800 mg strengths do not support the prescriber's titration plan or when the patient requires exclusion of a sensitizing excipient (dye, gluten, lactose, specific flavoring). Restricted under FDA essentially-a-copy guidance.
Compounded topical cream or gel	Typically 6% or 10% gabapentin; combination preparations per prescriber direction	Topical preparation for off-label localized peripheral neuropathic pain (post-amputation neuroma, postsurgical neuropathic pain in a localized distribution, vulvodynia, or small-area neuropathic conditions). Route is not commercially manufactured and is not subject to essentially-a-copy restriction. Evidence base is small case series and topical-analgesic reviews.
Manufactured immediate-release capsule, tablet, oral solution (reference product)	Neurontin 100, 300, 400 mg capsule; 600, 800 mg tablet; 250 mg/5 mL oral solution	FDA-approved manufactured Neurontin (Pfizer) and AB-rated generics. Titrated to 1800, 3600 mg/day in three divided doses for adult indications.
Manufactured gastric-retentive extended-release tablet (reference product)	Gralise 300, 600 mg tablet; titrated to 1800 mg once daily with the evening meal	FDA-approved manufactured Gralise (Almatica/ Assertio) for postherpetic neuralgia in adults.
Manufactured gabapentin enacarbil extended-release	Horizant 300, 600 mg tablet of gabapentin enacarbil prodrug; 600 mg once daily for restless	FDA-approved manufactured Horizant (gabapentin enacarbil, Arbor Pharmaceuticals). Prodrug actively transported across the entire small intestine and colon; produces dose-proportional gabapentin exposure.



Form	Concentration	Description
tablet (reference product)	legs syndrome, 600 mg twice daily for postherpetic neuralgia	

**Routes used in published literature:** oral, topical.

## ☼ Compounded Gabapentin Dosing

Route	Population	Range	Duration	Study type
Oral	Adults with postherpetic neuralgia (Neurontin labeled regimen)	Day 1: 300 mg; day 2: 600 mg in 2 divided doses; day 3: 900 mg in 3 divided doses; then titrate as needed to 1800 mg/day in 3 divided doses. Maximum studied dose: 3600 mg/day.	Indefinite while clinically beneficial	FDA-approved labeled regimen
Oral	Adults with partial-onset seizures (Neurontin labeled regimen, adjunctive)	Initiate at 300 mg three times daily; titrate to 900, 1800 mg/day in 3 divided doses. Doses up to 2400 mg/day used long-term; 3600 mg/day tolerated short-term.	Indefinite while clinically beneficial	FDA-approved labeled regimen
Oral	Pediatric patients 3, 12 years with partial seizures (Neurontin labeled regimen)	Initiate at 10, 15 mg/kg/day in 3 divided doses; titrate over approximately 3 days to effective dose. For 3, 4 year-olds, effective dose is 40 mg/kg/day; for 5, 12 year-olds, 25, 35 mg/kg/day.	Indefinite while clinically beneficial	FDA-approved labeled regimen
Oral	Adults with postherpetic neuralgia (Gralise labeled regimen)	Day 1: 300 mg; day 2: 600 mg; day 3: 900 mg; day 4: 1200 mg; day 5: 1500 mg; day 6 onwards: 1800 mg once daily with the evening meal.	Indefinite while clinically beneficial	FDA-approved labeled regimen
Oral	Adults with moderate-to-severe primary restless legs syndrome (Horizant labeled regimen)	600 mg once daily at approximately 5 pm. Doses above 600 mg/day do not provide additional benefit and increase adverse events.	Indefinite while clinically beneficial	FDA-approved labeled regimen
Oral	Adults with postherpetic neuralgia (Horizant labeled regimen)	Day 1, 3: 600 mg once daily in the morning; day 4 onwards: 600 mg twice daily (morning and afternoon).	Indefinite while clinically beneficial	FDA-approved labeled regimen



Route	Population	Range	Duration	Study type
Oral	Adults with painful diabetic peripheral neuropathy (off-label)	Titrate as for postherpetic neuralgia to 1800, 3600 mg/day in 3 divided doses	8 weeks in the pivotal trial; longer use as clinically indicated	Phase 3 RCT (off-label)
Oral	Adults with alcohol use disorder (off-label)	Gabapentin titrated to 1800 mg/day in 3 divided doses (900 mg/day arm also studied)	12 weeks in the pivotal trial	Phase 2 RCT (off-label)
Oral	Women with breast cancer and hot flashes (off-label)	900 mg/day in 3 divided doses (300 mg/day arm not significantly different from placebo)	8 weeks in the pivotal trial	Phase 3 RCT (off-label)
Topical	Adults with localized peripheral neuropathic pain (off-label, compounded)	Typically 6, 10% gabapentin cream or gel applied to the localized area three to four times daily; no labeled regimen	Per prescriber direction; reassess at 4, 8 weeks	Case series and topical-analgesic reviews (off-label)

Doctor-prescribed and titrated. Immediate-release gabapentin must be titrated upward over days because of dose-limiting sedation and dizziness during initiation; the labeled PHN escalation moves from 300 mg on day 1 to 1800 mg/day in 3 divided doses by approximately day 7 [fda\_label\_gralise]. Dose adjustment for renal impairment is required: at creatinine clearance 30, 59 mL/min, maximum daily dose is approximately 1400 mg; at 15, 29 mL/min, 700 mg; at <15 mL/min, 300 mg; and supplemental dosing is required after hemodialysis. Older adults are at increased risk of CNS adverse events and respiratory depression and warrant cautious initiation [fda\_label\_neurontin, fda\_safety\_2019].

Compounded preparations should mirror manufactured-product dosing unless the prescriber documents a patient-specific reason for variance. Gabapentin enacarbil (Horizant) cannot be substituted milligram-for-milligram for immediate-release gabapentin because of fundamentally different pharmacokinetics [lal2011, lal2013, cundy2010], and compounded preparations should not be cross-titrated from one manufactured product to another without explicit prescriber direction [fda\_label\_horizant]. Topical 6, 10% compounded gabapentin has no labeled regimen and is dosed per prescriber direction with reassessment at 4, 8 weeks [fda\_label\_gralise].

## ✓ Compounded Gabapentin Safety

Gabapentin's safety is dominated by central nervous system adverse events, somnolence, dizziness, fatigue, ataxia, and peripheral edema, that are dose-dependent and concentrated in the titration period. Rates in the Wiffen 2017 Cochrane review <sup>8</sup> are approximately: somnolence 14, 22%, dizziness 19, 29%, peripheral



edema 7, 8%, and gait disturbance 9% on gabapentin 1800, 3600 mg/day vs ~5, 8% on placebo. Adverse-event-driven discontinuation in chronic neuropathic pain trials runs 11, 13% on gabapentin vs ~9% on placebo.

Respiratory depression is the most clinically consequential safety concern. FDA's December 19, 2019 Drug Safety Communication <sup>32</sup> required new warnings on all gabapentinoid labels regarding serious breathing problems in patients using gabapentin with opioids or other CNS depressants, in patients with underlying respiratory impairment, and in elderly patients. Population-based Ontario data <sup>23 23</sup> reported that concomitant gabapentin and opioid use was associated with a 49% increase in opioid-related death (adjusted odds ratio 1.49; 95% CI 1.18, 1.88) compared with opioid use alone, with a dose-response gradient.

Misuse, abuse, and diversion are documented. Smith and colleagues (2016, *Addiction*) <sup>21</sup> systematically reviewed misuse and reported that gabapentin is misused for its sedative and euphorogenic effects, particularly among opioid-using populations, with prevalence of misuse in selected populations as high as 15, 22%; commentary by Dunlop (2016) <sup>22</sup> noted the clinical implications. Evoy and colleagues (2021, *J Clin Pharmacol*) reviewed the pharmacology of misuse liability <sup>25</sup> and Covvey and colleagues (2023) <sup>26</sup> surveyed pharmacist, prescriber, and policy expert opinions. As of 2026, gabapentin remains a non-controlled medication federally in the United States but is a scheduled drug in several states <sup>293031</sup>.

Other notable considerations include weight gain (in chronic neuropathic pain and anticonvulsant use), DRESS (drug reaction with eosinophilia and systemic symptoms; rare), suicidality (anticonvulsant class warning), and serious dermatologic reactions (rare). Gabapentin is generally well tolerated in older adults at appropriately reduced doses for renal function, but the increased risk of falls and confusion at any given exposure makes geriatric dose individualization important <sup>24</sup>. Manufactured-product safety data summarized here cannot be assumed to translate without modification to compounded preparations that differ in concentration, excipient profile, or route (especially topical), and FAERS pharmacovigilance evidence specific to compounded gabapentin is limited.

## Contraindications

Gabapentin is contraindicated only in patients with known hypersensitivity to gabapentin or any product excipient per the manufactured-product labels. For gabapentin enacarbil (Horizant), additional contraindications include hypersensitivity to gabapentin enacarbil <sup>31 2930</sup>.

Precautions include renal impairment (dose adjustment required), concomitant CNS depressants (opioids, benzodiazepines, alcohol) given the respiratory-depression signal <sup>32</sup>, older adults with compromised respiratory function, history of substance use disorder (given the documented misuse and diversion signal <sup>2125</sup>), and pregnancy (limited human data; potential developmental risk reported in animal studies) <sup>29</sup>. Suicidal ideation and behavior have been reported with anticonvulsants as a class.



## Drug interactions

Gabapentin is not metabolized by cytochrome P450 enzymes, is not protein-bound, and does not participate in CYP-mediated drug-drug interactions. The principal clinically important interactions are pharmacodynamic: additive sedation and respiratory depression with opioids, benzodiazepines, alcohol, and other CNS depressants <sup>3223</sup>. Antacids containing aluminum and magnesium reduce gabapentin bioavailability by approximately 20% if taken simultaneously; gabapentin should be administered at least 2 hours after antacid <sup>29</sup>.

Morphine increases gabapentin AUC by approximately 44% per labeling; this is clinically relevant given the additive respiratory depression risk. Hydrocodone exposure is reduced by gabapentin co-administration in a dose-dependent fashion. Patients on combination opioid and gabapentin regimens should be monitored for sedation and respiratory depression, and the combination should be avoided or minimized where clinically possible <sup>3223 293031</sup>.

## Adverse events

Across the pivotal Neurontin trials in postherpetic neuralgia <sup>35</sup>, painful diabetic peripheral neuropathy <sup>4</sup>, and partial seizures <sup>6</sup>, and the Cochrane 2017 meta-analysis <sup>8</sup>, the most common adverse events with gabapentin vs placebo were somnolence (14, 27%), dizziness (19, 29%), peripheral edema (7, 17%), ataxia/gait disturbance (3, 9%), fatigue (5, 11%), and nausea (4, 8%). Adverse-event-driven discontinuation in chronic neuropathic pain trials ran 11, 13% on gabapentin vs ~9% on placebo per the Cochrane synthesis <sup>8</sup>. Fibromyalgia trial discontinuation rates were similar <sup>9</sup>, and the alcohol-use-disorder trial reported tolerability comparable to placebo at 1800 mg/day <sup>11</sup>.

Serious adverse events specific to gabapentinoids include respiratory depression with concomitant CNS depressants <sup>3223</sup>, DRESS, multi-organ hypersensitivity, suicidality (anticonvulsant class effect), and rare angioedema. Misuse, abuse, and diversion are documented at population scale <sup>212526</sup> and FAERS pharmacovigilance for compounded gabapentin in particular is limited; pharmacist review at dispensing is the principal mitigation.

## ↗ Monitoring Compounded Gabapentin Therapy

Baseline assessment should include renal function (serum creatinine and creatinine clearance), concomitant medication review with particular attention to opioids, benzodiazepines, and other CNS depressants, screening for history of substance use disorder, and reproductive plans in patients of childbearing potential. In older adults, baseline assessment of fall risk and respiratory reserve is appropriate.

On therapy: tolerability assessment at each titration step; renal function periodically (especially in older adults and patients with chronic kidney disease); indication-specific response (pain score, seizure frequency, RLS symptom severity) at 4 and 8 weeks; review of concomitant CNS depressants and signs of



misuse or sedation [fda\_safety\_2019]. Patients should be educated to recognize and report excessive sedation, slowed breathing, mood or behavior changes, and unusual rash [fda\_label\_neurontin; fda\_label\_gralise; fda\_label\_horizant].

## 👤 Compounded Gabapentin in Special Populations

### ⚖️ Compounded Gabapentin Evidence Quality

Evidence supporting manufactured Neurontin, Gralise, and Horizant is mature: pivotal randomized trials in postherpetic neuralgia [rowbotham1998] and partial seizures [chadwick1998] supported the original Neurontin approvals, with subsequent phase 3 evidence for Gralise (gastric-retentive) and the Horizant prodrug program [rice2001]. The Cochrane 2017 systematic review and meta-analysis of gabapentin for chronic neuropathic pain in adults (37 studies, >5,900 participants) [wiffen2017] is the standard meta-analytic synthesis [hayes2012; smith2016]. Off-label evidence is large and variable in quality: pivotal RCTs support painful diabetic peripheral neuropathy [backonja1998], alcohol use disorder [mason2014], hot flashes in breast cancer survivors [pandya2005], fibromyalgia [arnold2007], and anxiety disorders [pande1999\_socphobia, pande2000\_panic], while randomized evidence does not support routine use for low back pain or sciatica [enke2018, mathieson2017].

Evidence specifically supporting compounded preparations is limited [evoy2021; covvey2023]. Oral suspensions and capsules can be expected to follow the saturable, dose-dependent absorption profile of immediate-release gabapentin [fda\_label\_neurontin] but compounded preparations are not bioequivalent to Neurontin and have not been characterized in formal PK studies [cundy2010; fda\_safety\_2019]. Topical 6, 10% compounded gabapentin for localized neuropathic pain is supported by small case series [boardman2008] and topical-analgesic reviews [knezevic2017] but has not been studied in adequately powered randomized trials and remains a tier 2, 3 off-label option [gomes2017]. Post-marketing safety considerations specific to the compounded supply chain include the same misuse, diversion, and concomitant-CNS-depressant respiratory-depression risks documented for manufactured gabapentin, plus the compounding-specific risks of dose-strength errors and excipient variability that any 503A preparation introduces [marson2007] [lal2011; lal2013].

### 📄 Major Compounded Gabapentin Clinical Studies

Study	Design	Participants	Duration	Finding
Rowbotham et al. (1998, JAMA), Pivotal RCT in	Phase 3, randomized, double-blind, placebo-controlled, multicenter	229	8 weeks	Average daily pain score reduced by 33% (from 6.3 to 4.2) on gabapentin vs 7.7% on placebo



Study	Design	Participants	Duration	Finding
postherpetic neuralgia	trial of gabapentin titrated to 3600 mg/day vs placebo in adults with postherpetic neuralgia			( $P < 0.001$ ); supported the 2002 FDA expansion of the Neurontin label to PHN [rowbotham1998]
Rice et al. (2001, Pain), Second independent PHN RCT	Phase 3, randomized, double-blind, placebo-controlled, multicenter trial of gabapentin 1800 mg/day or 2400 mg/day vs placebo in adults with postherpetic neuralgia	334	7 weeks	Mean weekly pain score reduced significantly more on gabapentin 1800 mg/day (-34.5%) and 2400 mg/day (-34.4%) vs placebo (-15.7%); replicates the Rowbotham 1998 effect at lower target doses [rice2001]
Backonja et al. (1998, JAMA), Pivotal RCT in painful diabetic peripheral neuropathy	Phase 3, randomized, double-blind, placebo-controlled, multicenter trial of gabapentin titrated to 3600 mg/day vs placebo in adults with painful diabetic peripheral neuropathy	165	8 weeks	Mean daily pain score reduced from 6.4 to 3.9 on gabapentin vs 6.5 to 5.1 on placebo ( $P < 0.001$ ); standard off-label evidence base for gabapentin in painful diabetic peripheral neuropathy (gabapentin not FDA-approved for this indication) [backonja1998]
Chadwick et al. (1998, Neurology), Monotherapy in newly diagnosed partial seizures	Phase 3, randomized, double-blind trial of gabapentin monotherapy in adults with newly diagnosed partial seizures (International Gabapentin Monotherapy Study Group 945-77)	292	26 weeks	Gabapentin 900, 1200, and 1800 mg/day produced comparable efficacy to active comparator, supporting partial-onset seizure efficacy as monotherapy [chadwick1998]
Marson et al. (2007, Lancet), SANAD partial epilepsy arm	Unblinded randomized controlled trial of carbamazepine, gabapentin, lamotrigine, oxcarbazepine, and topiramate for	1721	Up to 4 years follow-up	Gabapentin was inferior to lamotrigine on time-to-treatment-failure and time-to-12-month-remission composite outcomes; informs comparative effectiveness



Study	Design	Participants	Duration	Finding
	treatment of partial-onset epilepsy			positioning of gabapentin in partial epilepsy [marson2007]
Wiffen et al. (2017, Cochrane Database Syst Rev), Standard chronic neuropathic pain meta-analysis	Updated Cochrane systematic review and meta-analysis of gabapentin for chronic neuropathic pain in adults	5914 (37 studies)	4, 14 weeks pooled	Gabapentin at 1800, 3600 mg/day produces 50% or greater pain reduction in approximately 30, 40% of patients with postherpetic neuralgia or painful diabetic peripheral neuropathy vs 10, 20% with placebo (NNT ≈ 6, 8) [wiffen2017]. Moderate-quality evidence. Adverse-event-driven discontinuation 11, 13% on gabapentin vs ~9% placebo.
Mason et al. (2014, JAMA Internal Medicine), Gabapentin for alcohol use disorder	Phase 2 randomized, double-blind, placebo-controlled trial of gabapentin 900 mg/day vs 1800 mg/day vs placebo in adults with alcohol dependence	150	12 weeks	Dose-dependent increase in complete abstinence (4%, 11%, 17% on placebo, 900 mg, 1800 mg) and no-heavy-drinking days (23%, 30%, 45%); NNT 8 for abstinence and 5 for no heavy drinking at 1800 mg/day [mason2014]
Pandya et al. (2005, Lancet), Gabapentin for hot flashes in breast cancer	Phase 3 randomized, double-blind, placebo-controlled, three-arm trial of gabapentin 300 mg/day vs 900 mg/day vs placebo in women with breast cancer and ≥2 hot flashes/day	420	8 weeks	Hot flash severity score reduced by 46% on 900 mg/day vs 15% on placebo (P<0.001). The 300 mg/day arm did not differ significantly from placebo [pandya2005].
Arnold et al. (2007, Arthritis & Rheumatism), Gabapentin for fibromyalgia	Phase 2 randomized, double-blind, placebo-controlled, multicenter trial of gabapentin 1200, 2400 mg/day vs placebo in adults with fibromyalgia	150	12 weeks	51% of gabapentin-treated patients achieved 30% or greater improvement in Brief Pain Inventory average pain severity score vs 31% on placebo; modest tolerability issues at the higher dose range [arnold2007]
Pande et al. (1999, J Clin	Phase 2 randomized, double-blind, placebo-	69	14 weeks	Gabapentin reduced Liebowitz Social Anxiety Scale scores more



Study	Design	Participants	Duration	Finding
Psychopharmacol), Gabapentin for social phobia	controlled trial of gabapentin titrated to 900, 3600 mg/day vs placebo in adults with social phobia (social anxiety disorder)			than placebo; supports off-label use in social anxiety disorder (not FDA-approved for any anxiety indication) [pande1999_socphobia]
Pande et al. (2000, J Clin Psychopharmacol), Gabapentin for panic disorder	Phase 2 randomized, double-blind, placebo-controlled trial of gabapentin titrated to 600, 3600 mg/day vs placebo in adults with panic disorder	103	8 weeks	No overall benefit on the Panic and Agoraphobia Scale; pre-specified subgroup of more severely ill patients showed improvement on gabapentin [pande2000_panic]
Gee et al. (1996, J Biol Chem), Mechanism of action discovery	Radioligand binding and biochemical characterization of gabapentin binding in porcine brain membranes	—	—	Identified gabapentin as a high-affinity ligand of an auxiliary calcium channel subunit subsequently identified as $\alpha 2\delta$ -1; foundational mechanism paper [gee1996]
Sills (2006, Curr Opin Pharmacol), Mechanism review	Narrative review of $\alpha 2\delta$ -mediated mechanism of action for gabapentin and pregabalin	—	—	Consolidates the $\alpha 2\delta$ -1 binding evidence and downstream effects on presynaptic calcium influx and excitatory neurotransmitter release; standard mechanism reference [sills2006]
Lal et al. (2011, Int J Clin Pharmacol Ther), Gabapentin enacarbil $^{14}\text{C}$ disposition	Phase 1 single-dose study of the disposition of $^{14}\text{C}$ -radiolabeled gabapentin enacarbil in healthy male volunteers	6	Single dose	Characterized the absorption, conversion to gabapentin, and elimination of the gabapentin enacarbil prodrug; supports the dose-proportional PK that distinguishes Horizant from immediate-release Neurontin [lal2011]
Lal et al. (2013, J Clin Pharmacol), Population PK/PD of gabapentin enacarbil	Population pharmacokinetic and pharmacodynamic analysis after gabapentin enacarbil administration across	—	—	Linear dose-proportional gabapentin exposure after enacarbil prodrug administration; supports once-daily 600 mg dosing for RLS and



Study	Design	Participants	Duration	Finding
	phase 1 and phase 3 RLS programs			twice-daily 600 mg for postherpetic neuralgia [lal2013]
Hayes et al. (2012, <i>Ann Pharmacother</i> ), Gabapentin enacarbil for RLS review	Review of efficacy, safety, and pharmacology of gabapentin enacarbil (Horizant) for restless legs syndrome	—	—	600 mg once daily is the optimal labeled dose for moderate-to-severe primary RLS; doses above 600 mg/day do not add benefit [hayes2012]
Cundy et al. (2010, <i>Int J Clin Pharmacol Ther</i> ), Food effect on gabapentin enacarbil	Phase 1 randomized crossover study of food effect on gabapentin enacarbil pharmacokinetics	—	—	Gabapentin exposure increases with food fat content; supports the Horizant labeling requirement to administer with food [cundy2010]
Tiippana et al. (2007, <i>Anesth Analg</i> ), Perioperative gabapentinoids review	Systematic review of perioperative gabapentin and pregabalin for postoperative analgesia and opioid sparing	—	—	Modest opioid-sparing effects with increased sedation; informed subsequent FDA labeling on perioperative respiratory depression [tiippana2007]
Enke et al. (2018, <i>CMAJ</i> ), Anticonvulsants for low back pain meta-analysis	Systematic review and meta-analysis of nine RCTs of anticonvulsants (including gabapentin and pregabalin) for low back pain and lumbar radicular pain	859	Pooled trial durations	Gabapentinoids do not produce clinically meaningful benefit for low back pain or sciatica and increase adverse events; argues against routine use [enke2018]
Mathieson et al. (2017, <i>NEJM</i> ), Pregabalin for sciatica	Phase 3 randomized double-blind placebo-controlled trial of pregabalin (gabapentinoid class) for acute and chronic sciatica	209	8 weeks treatment, 52 weeks follow-up	No benefit on leg-pain intensity at 8 or 52 weeks; supports the negative conclusion of the Enke 2018 meta-analysis for the gabapentinoid class in radicular pain [mathieson2017]
Smith et al. (2016, <i>Addiction</i> ), Misuse, abuse, and diversion in	Systematic review of gabapentin misuse, abuse, and diversion in	—	—	Misuse documented particularly among opioid-using populations with prevalence as high as 15,



Study	Design	Participants	Duration	Finding
abuse, and diversion systematic review	clinical and general populations			22% in selected subgroups; informed subsequent state scheduling decisions and FDA safety communications [smith2016]
Gomes et al. (2017, PLoS Med), Gabapentin + opioid mortality (Ontario)	Population-based nested case-control study of opioid users in Ontario, Canada	1256 cases, 4619 controls	1997, 2013	Concomitant gabapentin and opioid use was associated with a 49% increase in the odds of opioid-related death (adjusted OR 1.49, 95% CI 1.18, 1.88) vs opioid use alone, with a dose-response gradient [gomes2017]
Goodman & Brett (2019, JAMA Internal Medicine), Off-label gabapentinoid use overview	Clinical overview of off-label use of gabapentinoid drugs in the United States	—	—	Documents wide off-label use, much of it not supported by adequate evidence; calls for more conservative prescribing and renewed attention to misuse and respiratory depression risk [goodman2019]
Evoy et al. (2021, J Clin Pharmacol), Gabapentinoid misuse pharmacology	Review of gabapentinoid pharmacology in the context of emerging misuse liability	—	—	Characterizes the pharmacologic substrate (CNS sedation, opioid potentiation) for misuse and recommends pharmacist-level interventions at dispensing [evoy2021]
Covvey et al. (2023, Res Social Adm Pharm), Pharmacist and prescriber survey	Mixed-methods survey of pharmacist, prescriber, and drug-policy expert opinions on gabapentinoid misuse and policy responses	—	—	Substantial concern across stakeholders about misuse and diversion, with widespread support for pharmacist-level screening and selective state scheduling [covvey2023]
Boardman et al. (2008, Obstet Gynecol), Topical gabapentin for vulvodynia	Retrospective case series of topical 2, 6% gabapentin compounded preparations in women with localized	51	Median 8 weeks	Symptomatic improvement in the majority of patients; provides the largest case-series support for topical compounded gabapentin in vulvodynia [boardman2008]



Study	Design	Participants	Duration	Finding
	and generalized vulvodynia			
Knezevic et al. (2017, Pain Management), Compounded topical analgesics review	Narrative review of single-agent and compounded topical analgesics including gabapentin, ketamine, amitriptyline, lidocaine, and baclofen for chronic neuropathic pain	—	—	Consolidates case-series evidence for topical compounded gabapentin alone and in combination preparations; identifies localized peripheral neuropathic pain as the principal indication and notes the limited evidence base [knezevic2017]
Dunlop (2016, Addiction), Smith commentary	Editorial commentary on the Smith 2016 systematic review of gabapentin misuse	—	—	Emphasizes the clinical implications of the misuse signal for prescribers and pharmacists and recommends screening before prescribing in populations with substance use history [dunlop2016]

## ⚠ Compounded Gabapentin Pharmacokinetics & Pharmacodynamics

### Pharmacokinetics

Immediate-release gabapentin (Neurontin) is absorbed by the saturable L-type amino acid transporter in the proximal small intestine, producing dose-dependent bioavailability that decreases from approximately 60% at 300 mg per dose to ~35% at 1600 mg per dose. Tmax is approximately 2, 3 hours after oral dosing; the drug is not bound to plasma proteins (<3%), is not metabolized, and is eliminated unchanged in the urine with clearance proportional to creatinine clearance and a half-life of 5, 7 hours [fda\_label\_neurontin] [cundy2010].

Gralise (gastric-retentive once-daily) achieves comparable steady-state AUC to divided-dose immediate-release gabapentin at 1800 mg/day with a different concentration-time profile that supports once-daily evening dosing [fda\_label\_gralise]. Gabapentin enacarbil (Horizant) is an actively transported prodrug absorbed across the entire small intestine and colon via MCT-1 and SMVT transporters; it is rapidly cleaved by non-specific carboxylesterases during absorption to gabapentin, producing dose-proportional gabapentin exposure that overcomes the saturable absorption of the parent drug [fda\_label\_horizant; lal2011; lal2013].



Compounded oral preparations should be assumed to follow the saturable absorption profile of immediate-release gabapentin and to require equivalent renal-impairment dose adjustment [cundy2010]. Topical 6, 10% compounded gabapentin has not been characterized in formal pharmacokinetic studies; systemic absorption from a small area of intact skin is typically negligible but cannot be assumed in damaged or inflamed skin, in occluded preparations, or at extremes of body-surface coverage.

## Pharmacodynamics

Pharmacodynamic effects are mediated by high-affinity binding to the  $\alpha 2\delta$ -1 auxiliary subunit of voltage-gated calcium channels in the central nervous system, with downstream reduction of presynaptic calcium influx and excitatory neurotransmitter release in sensitized nociceptive and epileptogenic circuits [gee1996, sills2006]. Clinically measured endpoints include pain score reduction (postherpetic neuralgia, painful diabetic peripheral neuropathy, fibromyalgia, hot flashes), seizure frequency (partial-onset epilepsy), RLS symptom severity (gabapentin enacarbil for primary RLS), and drinking outcomes (alcohol use disorder) [fda\_label\_neurontin].

Effects on sedation, dizziness, and ataxia are the principal dose-limiting pharmacodynamic effects and are typically concentrated in the titration period [fda\_label\_neurontin]. Tolerance to these effects develops in most patients over 1, 2 weeks at steady dose.

## ↕ Comparing Compounded Gabapentin Formulations

Three manufactured products are not interchangeable. Neurontin (immediate-release) requires three-times-daily dosing because of saturable absorption that limits per-dose bioavailability above approximately 600, 900 mg. Gralise (gastric-retentive) achieves comparable steady-state exposure to Neurontin at 1800 mg/day with once-daily evening dosing and a different concentration-time profile. Horizant (gabapentin enacarbil prodrug) is absorbed across the entire small intestine and colon, producing dose-proportional gabapentin exposure that supports 600 mg once daily for RLS or twice daily for PHN [fda\_label\_gralise; fda\_label\_horizant; lal2011].

Compounded oral preparations follow the immediate-release pharmacokinetic profile and are not bioequivalent to Gralise or Horizant. Clinicians should not substitute a compounded oral preparation for Gralise or Horizant without explicit re-titration. Topical 6, 10% compounded gabapentin is a distinct route with no commercial reference product and should be prescribed as a separate clinical entity rather than as a substitute for oral therapy [fda\_label\_neurontin; lal2013; cundy2010].

## 🔒 Compounded Gabapentin Storage and Handling

Manufactured Neurontin capsules and tablets are stored at controlled room temperature (20, 25°C). Neurontin oral solution is stored refrigerated at 2, 8°C [fda\_label\_neurontin]. Gralise and Horizant tablets



are stored at controlled room temperature [fda\_label\_gralise; fda\_label\_horizant]. Compounded oral suspensions, capsules, and topical preparations are stored per the pharmacy's stability data and assigned beyond-use date under USP <795> for nonsterile preparations [usp\_795]. Beyond-use dates for compounded gabapentin oral suspensions are typically 14, 90 days refrigerated depending on vehicle, preservative system, and supporting stability data.

Compounded preparations should be dispensed in the original pharmacy-labeled container with clear storage instructions; patients should be educated on refrigeration requirements for oral suspensions and on disposal of expired preparations.

## ☐ Compounded Gabapentin Compounding & Operations

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### 503A compounding

Compounded gabapentin is prepared under 503A on patient-specific prescriptions in state-licensed compounding pharmacies. RonanRx prepares nonsterile oral suspensions, capsules, and topical preparations per USP General Chapter <795> with documented active ingredient sourcing, gravimetric verification, beyond-use date assignment from supporting stability data, and lot traceability from API source through dispensing [usp\_795].

For oral preparations that are essentially copies of commercially available Neurontin (immediate-release capsule, tablet, or 250 mg/5 mL solution), the FDA section 503A essentially-a-copy guidance restricts compounding to documented patient-specific clinical needs the manufactured product cannot meet [fda\_essentially\_a\_copy] [fda503a]. Topical 6, 10% compounded gabapentin for localized neuropathic pain is a distinct route not commercially manufactured and is therefore not subject to the essentially-a-copy restriction. Custom-strength capsules to support an individualized titration step are evaluated case-by-case against the essentially-a-copy threshold.

Each batch is documented per state board of pharmacy retention rules with full traceability from API lot through dispensing, including ingredient identity verification, master formulation record, batch compounding record, and beyond-use date assignment basis [fda503a].

### Pharmacist review

Each prescription for compounded gabapentin undergoes pharmacist review prior to dispensing. The review confirms: a documented patient-specific clinical reason that the manufactured Neurontin, Gralise, or Horizant product is not appropriate (excipient sensitivity, dysphagia at a custom strength, individualized titration step, or topical localized use); appropriate renal-impairment dose adjustment per manufactured-product labels [fda\_label\_neurontin]; concomitant medication review with particular attention to opioids, benzodiazepines, and other CNS depressants given the FDA 2019 respiratory-depression safety communication [fda\_safety\_2019] and population-scale mortality evidence with opioids [gomes2017]; and



screening for history of substance use disorder given the documented misuse signal [smith2016, evoy2021, covvey2023] [fda\_label\_gralise; fda\_label\_horizant].

RonanRx does not fill prescriptions that read as routine substitution of compounded for manufactured product without documented clinical rationale, consistent with FDA guidance on compounded copies of commercially available drugs [fda\_essentially\_a\_copy] [fda\_label\_gralise]. Pharmacist clinical judgment is the principal mitigation against compounding-specific risks including dose-strength errors and excipient variability.

### Quality and traceability

Active pharmaceutical ingredients are sourced from FDA-registered facilities with documented certificates of analysis. Each compounded batch is recorded with lot numbers traceable to API source, compounding date, beyond-use date, supporting stability basis, and dispensing pharmacist of record. Finished product lot records are retained per state board of pharmacy retention requirements with master formulation records and batch compounding records available for inspection.

### Cold chain

Compounded gabapentin oral suspensions are typically refrigerated products with beyond-use dates of 14, 90 days depending on vehicle, preservative system, and supporting stability data. Refrigerated transport is used between the compounding pharmacy and the patient when required by the BUD assignment, with temperature monitoring through the shipment as applicable. Compounded capsules and topical preparations are typically stored at controlled room temperature and do not require cold-chain transport [usp\_795]. Manufactured Neurontin oral solution is the relevant cold-chain reference product [fda\_label\_neurontin].

## 🗨 Frequently Asked Questions About Compounded Gabapentin

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Is compounded gabapentin the same as Neurontin, Gralise, or Horizant?

No. Neurontin, Gralise, and Horizant are FDA-approved manufactured gabapentin products [fda\_label\_neurontin; fda\_label\_gralise; fda\_label\_horizant]. Compounded gabapentin is pharmacy-prepared on a patient-specific prescription and is not bioequivalent to the manufactured products. Compounded drugs are not FDA-approved [fda503a].

When is compounded gabapentin appropriate?

Three typical scenarios: (1) a pediatric or dysphagia patient who needs an oral suspension at a custom strength, excipient profile, or volume that the commercial Neurontin 250 mg/5 mL solution cannot meet; (2) a documented sensitivity to a dye, sweetener, or excipient in the manufactured product that requires a custom capsule or suspension; and (3) topical 6, 10% gabapentin cream or gel for off-label localized



peripheral neuropathic pain, a route that is not commercially manufactured [boardman2008; knezevic2017]. Cost or preference does not qualify under FDA section 503A [fda\_essentially\_a\_copy].

Does gabapentin work the same way as a GABA medication?

No. Despite the GABA structural similarity in its name, gabapentin does not bind GABA receptors. It binds the  $\alpha 2\delta$ -1 auxiliary subunit of voltage-gated calcium channels in the central nervous system, reducing calcium influx and excitatory neurotransmitter release in sensitized nerve pathways [gee1996]. The  $\alpha 2\delta$ -1 mechanism is shared with pregabalin (Lyrica) [sills2006].

What is gabapentin FDA-approved for?

Three approved indications across three products: (1) adjunctive therapy for partial-onset seizures in adults and pediatric patients  $\geq 3$  years (Neurontin); (2) postherpetic neuralgia in adults (Neurontin, Gralise, Horizant); and (3) moderate-to-severe primary restless legs syndrome in adults (Horizant only, the gabapentin enacarbil prodrug) [fda\_label\_neurontin; fda\_label\_gralise; fda\_label\_horizant]. Many other uses (diabetic neuropathy, fibromyalgia, hot flashes, alcohol use disorder, anxiety) are off-label but supported by randomized evidence.

How well does gabapentin work for nerve pain?

The Cochrane 2017 systematic review of 37 studies (>5,900 participants) reports that gabapentin 1800, 3600 mg/day produces 50% or greater pain reduction in approximately 30, 40% of patients with postherpetic neuralgia or painful diabetic peripheral neuropathy versus 10, 20% with placebo, a number-needed-to-treat of approximately 6, 8 for substantial benefit. Evidence is weaker in other neuropathic pain conditions and absent in low back pain and sciatica [wiffen2017; enke2018; mathieson2017].

Can gabapentin cause breathing problems?

Yes, particularly when combined with opioids, benzodiazepines, or alcohol, in older adults, and in patients with chronic obstructive pulmonary disease or other respiratory impairment. FDA's December 2019 Drug Safety Communication required new warnings on gabapentinoid labels for this risk. Ontario population data show a 49% increase in the odds of opioid-related death with concomitant gabapentin and opioids vs opioids alone [fda\_safety\_2019; gomes2017].

Is gabapentin addictive?

Gabapentin is not federally scheduled as a controlled substance in the United States but is a scheduled drug in several states. Misuse and diversion are documented at population scale, particularly among patients with opioid use disorder, who may use gabapentin to potentiate the effects of opioids [smith2016; evoy2021]. Pharmacist screening at dispensing is the principal mitigation [covvey2023].



## Does RonanRx sell compounded gabapentin directly to patients?

No. Compounded gabapentin requires a patient-specific prescription written by a licensed doctor for an identified patient with a documented clinical reason that the manufactured Neurontin, Gralise, or Horizant product is not appropriate, plus pharmacist review before dispensing [fda\_essentially\_a\_copy]. RonanRx is not a direct-to-consumer storefront [fda503a].

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## How to Access Compounded Gabapentin

Compounded Compounded Gabapentin is dispensed under 503A on a patient-specific prescription. Depending on your role, the next step looks different.



FOR PRESCRIBING CLINICIANS

### Offer this medication

A pharmacist will follow up within two business days. We'll cover state availability, supported formulations, and what integration looks like for your clinic.



[ronanrx.com/request-partnership-call](https://ronanrx.com/request-partnership-call)



PATIENT WITH A DOCTOR

### Receive your prescription

If your doctor has prescribed Compounded Gabapentin, sign up so we can prepare and ship your medication. The signup wizard collects intake and connects you to the prescribing workflow.



[ronanrx.com/patients](https://ronanrx.com/patients)



PATIENT WITHOUT A DOCTOR

### Find a partner clinic

RonanRx prescribes through partner clinics — we don't initiate prescriptions on this site. Read how the referral process works and how to find a partner clinic in your state.



[ronanrx.com/find-clinic](https://ronanrx.com/find-clinic)



## Other compounds RonanRx makes

This monograph is one of many in the RonanRx formulary. Every compound below is prepared under 503A on a patient-specific prescription. Browse the full catalog at [ronanrx.com/medications](https://ronanrx.com/medications) and [ronanrx.com/peptides](https://ronanrx.com/peptides), or scan the codes at right for each index.



Medications



Peptides

### MEDICATIONS (40)

Alpha-Lipoic Acid (ALA) – Antioxidant & mitochondrial  
 Coenzyme Q10 (CoQ10) – Antioxidant & mitochondrial  
 Glutathione – Antioxidant & mitochondrial  
 NAD+ / NMN – Antioxidant & mitochondrial  
 Compounded Topical Anesthetics (BLT, LET) – Dermatology  
 Topical Minoxidil – Dermatology  
 Topical Tretinoin – Dermatology  
 Compounded Magnesium – Energy & nutritional  
 Cyanocobalamin – Energy & nutritional  
 High-Dose Vitamin D – Energy & nutritional  
 Hydroxocobalamin – Energy & nutritional  
 Iron (Compounded) – Energy & nutritional  
 L-Carnitine – Energy & nutritional  
 Methylcobalamin (B12) – Energy & nutritional  
 Methylfolate – Energy & nutritional  
 Anastrozole – Hormone optimization  
 Clomiphene & Enclomiphene – Hormone optimization  
 DHEA – Hormone optimization  
 Estradiol – Hormone optimization  
 Estriol – Hormone optimization

Human Chorionic Gonadotropin (HCG) – Hormone optimization  
 Pregnenolone – Hormone optimization  
 Progesterone – Hormone optimization  
 Testosterone – Hormone optimization  
 Compounded Metformin – Metabolic & weight  
 Compounded Semaglutide – Metabolic & weight  
 Compounded Tirzepatide – Metabolic & weight  
 Lipotropic Injection (MIC, MICC) – Metabolic & weight  
 Low-Dose Naltrexone (LDN) – Metabolic & weight  
 Naltrexone-Bupropion Combination – Metabolic & weight  
 Topiramate – Metabolic & weight  
 Bremelanotide / PT-141 – Sexual health  
 Compounded Sildenafil – Sexual health  
 Compounded Tadalafil – Sexual health  
 Trimix Injection – Sexual health  
 Compounded Gabapentin – Sleep & recovery  
 Compounded Melatonin – Sleep & recovery  
 Compounded T3 (Liothyronine) – Thyroid  
 Compounded T3/T4 Combinations – Thyroid  
 Compounded T4 (Levothyroxine) – Thyroid



## PEPTIDES (21)

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**Sermorelin** — Available now

**Tesamorelin** — Available now

**AOD-9604** — Growth-hormone axis (under FDA review)

**CJC-1295** — Growth-hormone axis (under FDA review)

**GHRP-2 / GHRP-6** — Growth-hormone axis (under FDA review)

**Hexarelin** — Growth-hormone axis (under FDA review)

**Ipamorelin** — Growth-hormone axis (under FDA review)

**MK-677 / Ibutamoren** — Growth-hormone axis (under FDA review)

**5-Amino 1MQ** — Metabolic & longevity (under FDA review)

**Epitalon / Epithalon** — Metabolic & longevity (under FDA review)

**MOTS-C** — Metabolic & longevity (under FDA review)

**Thymosin Alpha-1 / Thymalin** — Metabolic & longevity (under FDA review)

**DSIP, Delta Sleep-Inducing Peptide** — Neuro & cognitive (under FDA review)

**Selank** — Neuro & cognitive (under FDA review)

**Semax** — Neuro & cognitive (under FDA review)

**Vasoactive Intestinal Peptide (VIP)** — Neuro & cognitive (under FDA review)

**BPC-157** — Tissue repair (under FDA review)

**KPV** — Tissue repair (under FDA review)

**LL-37** — Tissue repair (under FDA review)

**Pentadeca Arginate (PDA)** — Tissue repair (under FDA review)

**TB-500 / Thymosin Beta-4** — Tissue repair (under FDA review)

