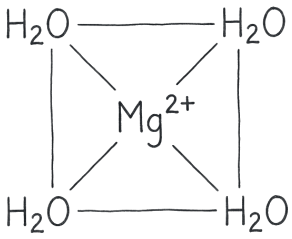
CLINICAL MONOGRAPH · ENERGY & NUTRITIONAL

Compounded Magnesium

Injectable magnesium for replacement and select clinical uses

Magnesium is a mineral your body needs for muscle, nerve, heart, and bone function. It is given as an IV drug for two specific emergencies, seizures in pre-eclampsia or eclampsia during pregnancy, and a dangerous heart rhythm called torsade de pointes, and it is also taken by mouth as a dietary supplement. Several different magnesium salts are used (sulfate, chloride, citrate, oxide, glycinate, malate, L-threonate), and they differ in how well they are absorbed and in side effects like diarrhea [tzivoni1988].

Most adults can get enough magnesium from food, but national surveys suggest a meaningful share of Americans do not. Magnesium has been studied for migraine prevention, acute asthma attacks, anxiety, and constipation, with varying levels of evidence [peikert1996; kew2014]. Newer forms like magnesium L-threonate are marketed for memory and brain health, but those claims so far rest mostly on mouse studies, not on robust human trials [magpie2002; rosanoff2012; slutsky2010].



EVIDENCE POSTURE FDA APPROVED WELL STUDIED REVIEWED **2026-05-11**

State-licensed 503A | Pharmacist reviewed | Doctor led | Cold-chain ready | Patient choice preserved

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FOR CLINICIANS

Magnesium is the fourth most abundant cation in the body and the second most abundant intracellular cation after potassium. It is a required cofactor for more than 300 enzymatic reactions including those involving ATP, serves as a physiologic voltage-dependent blocker of the NMDA glutamate receptor channel [nowak1984, mayer1984], stabilizes nucleic acid and membrane structure, and modulates calcium handling in cardiac and smooth muscle [debaaij2015, schwalfenberg2017]. Total body content is approximately 24 g; roughly 60% is in bone, 39% in soft tissue, and <1% in serum, which means serum magnesium is a poor index of total-body status [workinger2018].

Magnesium sulfate injection USP is FDA-approved for prevention and control of seizures in severe pre-eclampsia and eclampsia and for treatment of torsade de pointes and life-threatening hypomagnesemia. The Magpie Trial [magpie2002] randomized 10,141 women with pre-eclampsia to magnesium sulfate or placebo and reported a 58% reduction in eclampsia (relative risk 0.42; 95% CI 0.29-0.60). The Lucas trial [lucas1995] showed magnesium sulfate superior to phenytoin for eclampsia prevention. For torsade de pointes, magnesium sulfate IV bolus terminates polymorphic ventricular tachycardia even when serum magnesium is normal [tzivoni1988]. IV magnesium is also recommended for severe acute asthma exacerbations refractory to first-line therapy: the Cochrane review by Kew et al. [kew2014] and the 3Mg trial [goodacre2014] support a modest reduction in hospital admission for adults; the MAGNETIC pediatric trial [powell2013] and the Cochrane pediatric review [griffiths2016] support use in children with severe asthma not responding to standard therapy.

Oral magnesium is used for migraine prophylaxis at 400-600 mg elemental magnesium daily, supported by Peikert (1996) [peikert1996] and reviewed in Domitrz and Cegielska (2022) [domitrz2022]; for constipation as a saline cathartic (oxide, citrate, hydroxide) [mori2019]; and as nutritional replacement in documented hypomagnesemia. Evidence for depression, anxiety, sleep, and fibromyalgia is mixed: a randomized open-label trial of magnesium chloride [tarleton2017] showed reduction in depression symptoms at 6 weeks, and the Boyle et al. (2017) review [boyle2017] characterizes the anxiety/stress literature as suggestive but limited by trial quality. Magnesium L-threonate is marketed for cognitive benefit on the strength of Slutsky et al. (2010) [slutsky2010] in mice; human data remain sparse and brain-penetration claims should be framed as preclinical-only.

Compounded 503A magnesium roles include IV magnesium chloride or sulfate at custom concentrations for migraine and fibromyalgia infusion protocols, IM preparations at non-standard strengths, oral magnesium blends, and topical magnesium oil or cream, for which transdermal absorption evidence is weak and should not be assumed equivalent to oral or parenteral routes. Compounding does not duplicate FDA-approved manufactured magnesium sulfate injection without a documented clinical need consistent with FDA section 503A guidance.

Why Personalized Compounded Magnesium

The FDA-approved magnesium sulfate injection was reviewed for two narrow uses: eclampsia seizure prevention and torsade de pointes. Its labeled concentration and infusion rate were calibrated to obstetric and cardiac emergencies in adult patients with intact kidneys. They were not chosen for a fibromyalgia infusion protocol, a chronic migraine prophylaxis regimen, a pediatric severe asthma exacerbation, or an older patient on a loop diuretic with stage 3 chronic kidney disease. Magnesium's right dose depends on the indication, the route, the patient's baseline magnesium status (which serum levels poorly reflect), renal function, and the medications the patient already takes, including aminoglycosides, neuromuscular blockers, and PPIs. None of that lives in the package insert.

Compounding closes that gap. A 503A pharmacy can prepare IV magnesium sulfate or magnesium chloride at non-standard concentrations for a migraine or fibromyalgia infusion protocol, IM strengths outside the commercial range, preservative-free formulations for patients who react to sulfite excipients, and oral blends that combine well-absorbed salts (glycinate, malate) with a clinically chosen elemental dose that no single OTC product provides. The molecule is the same Mg ion the FDA reviewed in magnesium sulfate injection USP, the change is the strength, the salt, the route, and what gets left out, all tailored to one patient and one prescription.

This is what pharmacy looked like before mass manufacturing. A doctor wrote the prescription, a pharmacist prepared it for that patient, and the patient's name was on the label. Compounded magnesium is that older arrangement, kept honest by state-board inspection and pharmacist accountability.

Quick Facts About Compounded Magnesium

Category: Essential divalent intracellular cation; NMDA receptor antagonist; cofactor for >300 enzymatic reactions including ATP-dependent processes

Active ingredient: Magnesium ion (Mg^{2+}), dispensed as multiple salts: sulfate (IV/IM), chloride, citrate, oxide, glycinate (bisglycinate), malate, L-threonate

FDA-approved forms: Magnesium sulfate injection USP (IV/IM), FDA-approved for prevention/control of seizures in pre-eclampsia and eclampsia, and for treatment of torsade de pointes and life-threatening hypomagnesemia. Multiple oral magnesium salts are sold OTC as dietary supplements (not FDA-approved drug products).

Routes: Intravenous, intramuscular, oral, topical/transdermal

Evidence posture: FDA-approved IV use is supported by large RCTs (Magpie Trial, Eclampsia Trial). Migraine prophylaxis with oral salts and IV magnesium for acute severe asthma are well-studied. Transdermal absorption and magnesium L-threonate brain-penetration claims rest on limited human data; threonate evidence is primarily preclinical mouse work.

Compounded under: 503A, patient-specific prescriptions for IV/IM custom concentrations, oral blends, or strengths not available as a manufactured drug product. Compounding does not duplicate any FDA-approved manufactured magnesium sulfate injection without documented clinical need.

OTC overlap: Oral magnesium salts (citrate, oxide, glycinate, malate, threonate) are broadly available as dietary supplements. Compounded oral preparations are appropriate only when a specific strength, combination, or excipient profile cannot be obtained from an OTC product.

SPECIALS: PATIENT-SPECIFIC PRESCRIPTION ONLY

Compounded Magnesium 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 Magnesium?

Magnesium is the ninth most abundant element in the universe and an essential dietary mineral for humans. The body of a 70-kg adult contains approximately 24 g (1 mol) of magnesium, of which about 60% is in bone, 39% in soft tissue (predominantly skeletal muscle), and less than 1% in serum and red blood

cells. Normal serum magnesium ranges from approximately 0.75-0.95 mmol/L (1.8-2.3 mg/dL); ionized (biologically active) serum magnesium is approximately 55-70% of total. Serum is a poor surrogate for intracellular and total-body status because magnesium homeostasis defends the serum compartment last [debaaij2015, workinger2018].

In clinical use, magnesium is dispensed as multiple salts that differ in solubility, oral bioavailability, gastrointestinal tolerability, and indications. The parenteral form is magnesium sulfate (USP), supplied as a 50% solution (500 mg/mL ≈ 4 mEq/mL elemental Mg) and as premixed 1, 2, and 4 g/100 mL infusion bags. Oral salts in common use are magnesium oxide (high elemental content, low oral bioavailability, cathartic effect), magnesium citrate (moderate bioavailability, used for bowel prep), magnesium chloride (moderate bioavailability), magnesium glycinate / bisglycinate (well-tolerated, lower GI effect), magnesium malate, and magnesium L-threonate. Compounded preparations include sterile IV/IM magnesium sulfate or chloride at custom concentrations and oral capsule or powder blends [grober2015].

Magnesium is recognized as a public-health relevant nutrient. National Health and Nutrition Examination Survey (NHANES) data analyzed by Rosanoff and colleagues [rosanoff2012] documented that approximately half of U.S. adults consume less than the Estimated Average Requirement for magnesium, with intake patterns particularly low in older adults, in Black and Hispanic populations, and in those with low fruit, vegetable, nut, legume, and whole-grain consumption. Subclinical magnesium inadequacy has been linked epidemiologically to hypertension, type 2 diabetes, metabolic syndrome, and cardiovascular events [dinicolantonio2018, chiuve2011], although causal inference from these observational data is limited.

How Compounded Magnesium Works

Magnesium has four well-characterized mechanisms relevant to clinical use. First, it is the obligate cofactor for ATP, the biologically active form of adenosine triphosphate is the Mg-ATP complex, and for more than 300 enzymatic reactions including kinases, polymerases, and synthetases [debaaij2015, schwalfenberg2017]. Second, it serves as the physiologic voltage-dependent blocker of the NMDA glutamate receptor cation channel: at resting membrane potentials Mg^{2+} occupies the channel pore, and channel opening requires both glutamate binding and membrane depolarization to relieve the magnesium block [nowak1984, mayer1984]. This NMDA-blocking action underlies magnesium's anticonvulsant effect in eclampsia, its mechanistic rationale for migraine prophylaxis, and its central nervous system effects more broadly.

Third, magnesium acts as a natural calcium-channel antagonist: it competes with calcium at L-type voltage-gated calcium channels in vascular and cardiac smooth muscle, producing vasodilation and modulating cardiac conduction. This mechanism underlies the use of magnesium sulfate in pre-eclampsia (where cerebral vasospasm contributes to seizure risk) and in torsade de pointes (where magnesium suppresses early afterdepolarizations that trigger the arrhythmia) [tzivoni1988]. Fourth, magnesium stabilizes

membranes and nucleic acids electrostatically and is required for K^+ retention by the Na/K-ATPase, hypomagnesemia commonly drives refractory hypokalemia and contributes to cardiac arrhythmia susceptibility.

Bronchial smooth muscle relaxation by magnesium, the mechanistic basis for IV magnesium in acute severe asthma, combines calcium antagonism with inhibition of acetylcholine release at neuromuscular junctions and a direct effect on cAMP signaling. The effect is observable at supraphysiologic serum concentrations achieved with 2 g IV magnesium sulfate over 20 minutes [kew2014, goodacre2014].

Biological Role of Compounded Magnesium

Magnesium is the second most abundant intracellular cation after potassium and the obligate cofactor for the active form of ATP. Every reaction that hydrolyzes or transfers a phosphate from ATP requires magnesium. This places magnesium at the center of energy metabolism, nucleic acid synthesis, protein synthesis, and ion transport, including the Na/K-ATPase that maintains the resting membrane potential. Skeletal muscle, cardiac muscle, and the central nervous system are particularly magnesium-dependent tissues [debaaij2015].

Whole-body magnesium homeostasis is maintained by intestinal absorption (passive paracellular plus active transcellular TRPM6/TRPM7-mediated transport), renal handling (60% reabsorbed in the thick ascending limb via the paracellin-1 pathway, with fine control in the distal convoluted tubule), and exchange with the bone reservoir. The kidney is the dominant control point; renal magnesium wasting from loop diuretics, thiazide diuretics, proton pump inhibitors, alcohol, and uncontrolled diabetes is a common driver of clinical hypomagnesemia. Because serum magnesium is the smallest pool and the last to fall, normal serum magnesium does not exclude intracellular or total-body depletion [workinger2018, schwalfenberg2017].

Detailed Mechanism of Compounded Magnesium

Mg^{2+} regulates cellular function through both direct ion-channel interactions and through its requirement for nucleotide handling. The NMDA receptor channel has been a focus since the seminal 1984 work by Nowak et al. [nowak1984] and Mayer et al. [mayer1984], who independently demonstrated that extracellular Mg^{2+} at physiologic concentrations produces a voltage-dependent block of NMDA channels in central neurons. The block is relieved by depolarization, making NMDA channels coincidence detectors for presynaptic glutamate release and postsynaptic depolarization, the cellular basis for long-term potentiation and synaptic plasticity. Pharmacologically, raising extracellular magnesium reinforces this block and reduces NMDA-mediated excitotoxicity, neuronal hyperexcitability, and (in the pregnant brain) the cerebral component of eclamptic seizure risk.

Magnesium L-threonate was developed on the basis of preclinical work by Slutsky and colleagues [slutsky2010] showing that oral threonate salt elevated cerebrospinal fluid magnesium in rats and enhanced learning and memory in aged mice. The implication, marketed broadly in the supplement industry, is that threonate provides preferential brain magnesium delivery. The translational reach of this claim is limited: human RCT data demonstrating cognitive benefit are sparse, no FDA approval exists for any threonate indication, and the original work has not been independently reproduced at scale. RonanRx frames threonate brain-penetration claims as preclinical-only and not as established human benefit.

In cardiac physiology, magnesium acts as a natural calcium antagonist at L-type voltage-gated calcium channels, stabilizes the resting membrane potential by supporting Na/K-ATPase and inward-rectifier K^+ channels, and suppresses early afterdepolarizations during the plateau and repolarization phases of the action potential. These effects underlie the use of magnesium sulfate in torsade de pointes [tzivoni1988], where IV magnesium 1-2 g bolus terminates polymorphic VT even in the setting of normal serum magnesium. The preventive use of perioperative magnesium in cardiac surgery for atrial fibrillation prophylaxis was supported by the Burgess et al. meta-analysis (2006) [burgess2006] but a subsequent 2013 meta-analysis by Cook et al. [cook2013] reported that prophylactic magnesium did not prevent post-cardiac-surgery atrial fibrillation in their pooled analysis, leaving practice mixed.

In bronchial smooth muscle, magnesium produces relaxation through calcium-channel antagonism, inhibition of acetylcholine release at the neuromuscular junction, and stabilization of mast cells. The clinically relevant exposure is achieved by 2 g IV magnesium sulfate over 20 minutes, which produces a brief supraphysiologic plasma magnesium peak. The pediatric MAGNETIC trial of nebulized magnesium [powell2013] tested whether the inhaled route reproduces the bronchodilator effect; the trial reported a modest improvement in asthma severity score but did not establish nebulized magnesium as a standard-of-care intervention.

Compounded Magnesium Research History

The medicinal use of magnesium salts dates to the 17th-century Epsom salt (magnesium sulfate heptahydrate) preparations. Modern clinical magnesium therapy begins with the early 20th-century use of intravenous and intramuscular magnesium sulfate in obstetrics for eclampsia, championed in the U.S. by Lazard and later by Pritchard's Parkland Memorial protocol. The Eclampsia Trial Collaborative Group's 1995 work demonstrated magnesium sulfate's superiority over both diazepam and phenytoin in established eclampsia; Lucas and colleagues [lucas1995] published the parallel NEJM trial showing magnesium sulfate superior to phenytoin for prophylaxis against eclampsia in pre-eclamptic women. The Magpie Trial [magpie2002], the largest randomized trial of magnesium for any indication, randomized 10,141 women with pre-eclampsia to magnesium sulfate vs placebo and reported a 58% reduction in eclampsia incidence with no clear effect on maternal mortality. Belfort et al. (2003) [belfort2003] subsequently demonstrated magnesium sulfate superior to nimodipine, ending the calcium-channel-blocker challenge to magnesium for eclampsia prevention.

The neurophysiology of magnesium took shape with the 1984 work of Nowak et al. [nowak1984] and Mayer et al. [mayer1984], who established that extracellular Mg^{2+} produces voltage-dependent block of the NMDA glutamate receptor, a foundational discovery for understanding synaptic plasticity, excitotoxicity, and the mechanism of magnesium's anticonvulsant action in eclampsia. Cardiac magnesium therapy advanced with the 1988 report by Tzivoni et al. [tzivoni1988] demonstrating IV magnesium sulfate as effective treatment for torsade de pointes, and through subsequent decades of work on magnesium and perioperative atrial fibrillation prevention; the Burgess et al. meta-analysis (2006) [burgess2006] reported a benefit, while Cook et al. (2013) [cook2013] in a more recent pooled analysis did not, leaving the cardiothoracic prophylaxis question contested.

Migraine research established magnesium as a plausible prophylactic agent through Facchinetti et al. (1991) [facchinetti1991] (menstrual migraine), Peikert et al. (1996) [peikert1996] (oral magnesium prophylaxis), and Mauskop et al. (1995) [mauskop1995] (IV magnesium for acute attacks with low ionized magnesium). The Mauskop and Altura (1998) review [mauskop1998] consolidated the migraine evidence; the Demirkaya et al. (2001) trial [demirkaya2001] established IV magnesium sulfate's role in treating acute migraine; and the Domitrz and Cegielska (2022) review [domitrz2022] synthesized the contemporary evidence base. Acute asthma research culminated in the Kew Cochrane review (2014) [kew2014], the 3Mg trial [goodacre2014] [goodacre2014], the pediatric MAGNETIC trial [powell2013] [powell2013], and the Griffiths/Kew pediatric Cochrane review (2016) [griffiths2016].

Magnesium L-threonate was introduced on the basis of preclinical mouse data from Slutsky et al. (2010) in Neuron [slutsky2010], who reported that the threonate salt elevated rodent CSF magnesium and enhanced learning and memory in aged mice. Translation to human cognitive benefit remains incomplete and the supplement marketing claims around brain magnesium frequently overstate the evidence. Magnesium and depression / anxiety research has produced suggestive but limited human trial evidence, Eby and Eby (2006) [eby2006] reported rapid recovery in case-series form, Serefko et al. (2013) [serefko2013] reviewed the preclinical mechanism, Tarleton et al. (2017) [tarleton2017] reported a randomized open-label crossover trial of magnesium chloride for mild-to-moderate depression, and Boyle et al. (2017) [boyle2017] characterized the anxiety/stress literature as suggestive but limited by methodologic quality. Mori et al. (2019) [mori2019] published a randomized double-blind placebo-controlled trial of magnesium oxide for chronic constipation, supporting the long-standing OTC use.

Compounded Magnesium Timeline

1984 • Nowak et al [nowak1984]. (Nature) and Mayer et al [mayer1984]. (Nature) independently establish that extracellular Mg^{2+} produces voltage-dependent block of the NMDA glutamate receptor, foundational neurophysiology for magnesium's anticonvulsant and neurologic effects

1988 • Tzivoni et al [tzivoni1988]. (Circulation), IV magnesium sulfate as effective treatment for torsade de pointes polymorphic ventricular tachycardia

1991 • Facchinetti et al [facchinetti1991]. (Headache), oral magnesium prophylaxis for menstrual migraine demonstrates intracellular magnesium and symptom effects

1995 • Lucas et al [lucas1995]. (NEJM), magnesium sulfate superior to phenytoin for prevention of eclampsia in women with pre-eclampsia

1995 • Mauskop et al [mauskop1995]. (Clin Sci), IV magnesium sulfate relieves migraine attacks in patients with low serum ionized magnesium

1996 • Peikert et al [peikert1996]. (Cephalalgia), oral magnesium 600 mg daily reduces migraine frequency vs placebo in a 12-week prospective multicenter RCT

1998 • Mauskop and Altura (Clin Neurosci), review of magnesium in migraine pathogenesis and treatment consolidating the 1990s evidence [mauskop1998]

2001 • Demirkaya et al [demirkaya2001]. (Headache), IV magnesium sulfate 1 g for acute migraine attacks improves pain and associated symptoms

2002 • Magpie Trial Collaborative Group (Lancet), N=10,141 randomized trial reports 58% reduction in eclampsia with magnesium sulfate vs placebo in women with pre-eclampsia [magpie2002]

2003 • Belfort et al [belfort2003]. (NEJM), magnesium sulfate superior to nimodipine for prevention of eclampsia, ending the calcium-channel-blocker challenge

2006 • Eby and Eby (Med Hypotheses), case series of rapid recovery from major depression with magnesium treatment; small, uncontrolled [eby2006]

2006 • Burgess et al [burgess2006]. (Eur Heart J), meta-analysis of interventions for post-operative atrial fibrillation after cardiac surgery: pooled estimate favors prophylactic magnesium

2010 • Slutsky et al [slutsky2010]. (Neuron), magnesium L-threonate elevates rodent CSF magnesium and enhances learning and memory in aged mice; commercial threonate supplements derive from this preclinical work

2011 • Chiuve et al [chiuve2011]. (Am J Clin Nutr), prospective cohort: higher plasma and dietary magnesium associated with lower risk of sudden cardiac death in women

2012 • Rosanoff et al [rosanoff2012]. (Nutr Rev), NHANES-derived analysis: approximately half of U.S. adults consume less than the Estimated Average Requirement for magnesium

2013 • Powell et al [powell2013]. MAGNETIC trial (Lancet Respir Med), nebulized magnesium sulfate in children with severe acute asthma improves asthma severity score modestly

2013 • Cook et al [cook2013]. (Ann Thorac Surg), updated meta-analysis: prophylactic magnesium does not prevent atrial fibrillation after cardiac surgery, contradicting earlier pooled estimates

2013 • Serefko et al [serefko2013]. (Pharmacol Rep), review of magnesium in depression: preclinical mechanism plus limited human data

2014 • Kew et al [kew2014]. Cochrane review (Cochrane Database Syst Rev), IV magnesium sulfate reduces hospital admission in adults with acute severe asthma not responding to standard therapy

2014 • Goodacre et al [goodacre2014]. 3Mg trial (Health Technol Assess), IV and nebulized magnesium sulfate vs placebo in adults with acute severe asthma in the emergency department

2015 • de Baaij, Hoenderop, Bindels (Physiol Rev), comprehensive review of magnesium in human health and disease [debaaij2015]

2015 • Gröber et al [grober2015]. (Nutrients), review of magnesium in prevention and therapy

2016 • Griffiths and Kew Cochrane review (Cochrane Database Syst Rev), IV magnesium sulfate for children with acute asthma in the emergency department [griffiths2016]

2016 • Zhang et al [zhang2016]. (Hypertension), meta-analysis of oral magnesium supplementation and blood pressure in randomized double-blind placebo-controlled trials

2017 • Schwalfenberg and Genuis (Scientifica), clinical review on the importance of magnesium in healthcare [schwalfenberg2017]

2017 • Tarleton et al [tarleton2017]. (PLoS One), randomized open-label crossover trial of magnesium chloride 248 mg daily for mild-to-moderate depression

2017 • Boyle et al [boyle2017]. (Nutrients), systematic review of magnesium supplementation on subjective anxiety and stress: suggestive but limited by trial quality

2018 • DiNicolantonio et al [dinicolantonio2018]. (Open Heart), review framing subclinical magnesium deficiency as a cardiovascular and public-health concern

2018 • Workinger et al [workinger2018]. (Nutrients), challenges in the diagnosis of magnesium status; serum magnesium is a poor indicator of total-body content

2019 • Mori et al [mori2019]. (J Neurogastroenterol Motil), randomized double-blind placebo-controlled trial of magnesium oxide 1.5 g/day for chronic constipation: improved bowel-movement frequency and stool form

2022 • Domitrz and Cegielska (Nutrients), review of magnesium in migraine pathogenesis and treatment [domitrz2022]

Clinical Contexts for Compounded Magnesium

Prevention and control of seizures in severe pre-eclampsia and eclampsia FDA APPROVED

FDA-approved indication for magnesium sulfate injection.

Magnesium sulfate IV/IM is the standard-of-care anticonvulsant for severe pre-eclampsia and eclampsia. The Magpie Trial [magpie2002] randomized 10,141 women with pre-eclampsia (BP ≥140/90 with proteinuria) to magnesium sulfate vs placebo and reported a 58% relative-risk reduction in eclampsia (RR 0.42; 95% CI 0.29-0.60) without clear effect on maternal mortality. Lucas et al. [lucas1995] demonstrated superiority over phenytoin in NEJM, and Belfort et al. [belfort2003] subsequently showed superiority over nimodipine. The Pritchard regimen (4-6 g IV load over 15-20 minutes followed by 1-2 g/hour IV infusion) and the Zuspan regimen (4 g IV load followed by 1-2 g/hour) are both in widespread obstetric use.

Branded product: Magnesium Sulfate Injection USP

Torsade de pointes and life-threatening polymorphic ventricular tachycardia FDA APPROVED

FDA-approved indication for magnesium sulfate injection.

IV magnesium sulfate 1-2 g bolus terminates torsade de pointes polymorphic VT even in the setting of normal serum magnesium [tzivoni1988]. The action is attributed to suppression of early afterdepolarizations during the action-potential plateau and to calcium-channel antagonism. Magnesium is also recommended for digitalis-induced ventricular arrhythmia and for refractory ventricular tachycardia in the setting of hypomagnesemia.

Branded product: Magnesium Sulfate Injection USP

Symptomatic hypomagnesemia and electrolyte replacement FDA APPROVED

FDA-approved indication for magnesium sulfate injection.

IV magnesium sulfate is indicated for treatment of symptomatic hypomagnesemia (serum Mg <1.2 mg/dL or symptomatic at higher levels), including tetany, neuromuscular irritability, and arrhythmia in the setting of magnesium depletion. Repletion typically requires 1-2 g IV magnesium sulfate over 30-60 minutes for moderate deficits and up to 4-6 g over 8-24 hours for severe deficits, titrated to serum magnesium and reflex monitoring. Concurrent hypokalemia and hypocalcemia frequently coexist and may not correct until magnesium is replaced [debaaij2015, workinger2018].

Branded product: Magnesium Sulfate Injection USP

Acute severe asthma exacerbation refractory to first-line therapy WELL STUDIED

Well-studied adjunctive use; not a separate FDA labeled indication.

IV magnesium sulfate 2 g over 20 minutes is recommended for adults with acute severe asthma not responding to inhaled β2-agonists, ipratropium, and systemic corticosteroids. The Cochrane review by Kew et al. [kew2014] pooled 14 RCTs and reported a reduction in hospital admission. The 3Mg trial [goodacre2014] tested both IV and nebulized magnesium and reported modest benefit on physiologic endpoints. In children, the MAGNETIC trial [powell2013] supported nebulized magnesium for severe acute asthma, and the Griffiths and Kew Cochrane review [griffiths2016] supported IV magnesium for children not responding to standard therapy.

Migraine prophylaxis WELL STUDIED

Well-studied oral indication; supported by RCT evidence and contemporary review.

Oral magnesium at 400-600 mg elemental magnesium daily is supported for migraine prophylaxis by Peikert et al. [peikert1996], who reported a reduction in attack frequency vs placebo over 12 weeks with magnesium dicitrate 600 mg/day. Facchinetti et al. [facchinetti1991] demonstrated efficacy specifically for menstrual migraine. The Domitrz and Cegielska review [domitrz2022] and the Mauskop and Altura review [mauskop1998] consolidate the literature. The American Academy of Neurology and American Headache Society guidelines list magnesium as Level B (probably effective) for migraine prevention.

Acute migraine attack WELL STUDIED

Well-studied IV indication; small RCT evidence base.

IV magnesium sulfate 1 g over 15 minutes was studied by Demirkaya et al. [demirkaya2001] in adults with acute migraine and produced significant pain reduction and improvement in associated symptoms vs placebo. Mauskop et al. [mauskop1995] reported that IV magnesium was particularly effective in patients with low serum ionized magnesium at presentation. The clinical role is as second-line therapy when triptans and standard analgesics are insufficient or contraindicated.

Constipation and bowel preparation WELL STUDIED

Well-established OTC use; randomized trial evidence for chronic constipation.

Magnesium oxide and magnesium citrate exert a saline-cathartic effect through osmotic retention of intestinal water. Mori et al. [mori2019] randomized adults with chronic constipation to magnesium oxide 1.5 g daily vs placebo and reported improved bowel-movement frequency and stool form at 4 weeks. Magnesium citrate is widely used as a colonoscopy preparation agent. These uses are dose-limited by diarrhea, the most common adverse effect of high-dose oral magnesium.

Post-operative atrial fibrillation prevention after cardiac surgery WELL STUDIED

Studied with conflicting meta-analytic conclusions.

Burgess et al. [burgess2006] reported a pooled benefit of prophylactic magnesium for post-cardiac-surgery atrial fibrillation in a 2006 meta-analysis. A subsequent 2013 pooled analysis by Cook et al. [cook2013] reported that prophylactic magnesium did not reduce post-cardiac-surgery atrial fibrillation. The literature is therefore mixed; some cardiothoracic protocols include perioperative magnesium and others do not.

Depression, adjunctive supplementation EMERGING

Limited evidence; small open-label trial and case-series data only.

Tarleton et al. [tarleton2017] reported a 6-week randomized open-label crossover trial of magnesium chloride 248 mg elemental daily in adults with mild-to-moderate depression and observed clinically meaningful reduction in PHQ-9 scores. Eby and Eby [eby2006] published a case-series report of rapid recovery from major depression with magnesium treatment. The Serefko et al. [serefko2013] review consolidated preclinical mechanism and limited human data. The overall evidence base is preliminary; magnesium is not a substitute for standard depression therapy.

Anxiety and stress, oral supplementation EMERGING

Limited evidence; review characterizes literature as suggestive but methodologically limited.

The Boyle et al. [boyle2017] systematic review of 18 studies of magnesium supplementation for subjective anxiety and stress concluded that the literature is suggestive of benefit in subpopulations with elevated anxiety symptoms but is limited by small sample sizes, heterogeneous populations, and methodologic quality. Magnesium is not a substitute for established anxiolytic therapy.

Blood pressure reduction WELL STUDIED

Studied in oral-supplementation meta-analysis; modest effect size.

Zhang et al. [zhang2016] meta-analyzed 34 randomized double-blind placebo-controlled trials of oral magnesium supplementation and reported a modest reduction in systolic and diastolic blood pressure (approximately 2 mmHg systolic, 1.8 mmHg diastolic) with median dose 368 mg/day for median 3 months. The effect is small but additive to other interventions and is most evident in magnesium-deficient subgroups.

Cognitive function, magnesium L-threonate PRECLINICAL

Preclinical mouse data only; human evidence sparse. Marketed widely as a brain-magnesium supplement.

Slutsky et al. [slutsky2010] reported in Neuron that oral magnesium L-threonate elevated rodent CSF magnesium and enhanced learning and memory in aged mice. This preclinical finding is the basis for commercial threonate supplements marketed for brain health. Human randomized controlled trials demonstrating cognitive benefit at scale are lacking. RonanRx frames threonate brain-penetration claims as preclinical-only and not as established human benefit.

Off-Label Uses of Compounded Magnesium

Fibromyalgia infusion protocols EMERGING

Off-label; uncontrolled or small-cohort evidence only.

Custom IV magnesium chloride or sulfate infusions at variable concentrations are administered in some integrative-medicine and pain-management practices for fibromyalgia and chronic-fatigue presentations [grober2015]. Published evidence is limited to small uncontrolled cohorts; RCT-grade efficacy is not established. Patient selection, monitoring, and a documented clinical rationale are required.

Transdermal magnesium for muscle pain or nocturnal cramps PRECLINICAL

Off-label; transdermal absorption evidence is weak.

Topical magnesium oil (saturated magnesium chloride solution) and magnesium-containing creams are marketed for muscle aches, restless legs, and sleep. Transdermal absorption of magnesium through intact skin is poorly characterized and the small available human studies do not establish that meaningful systemic magnesium levels are achieved. Compounded topical magnesium is dispensed at RonanRx only when the prescriber documents specific local-effect rationale; systemic-effect claims for transdermal magnesium should be framed as unproven [grober2015].

FDA-Approved Uses of Compounded Magnesium

Brand	Indication	Year	Route
Magnesium Sulfate Injection USP (multiple generic manufacturers)	Prevention and control of seizures in severe pre-eclampsia and eclampsia; treatment of torsade de pointes and life-threatening hypomagnesemia	—	Intravenous or intramuscular

Magnesium sulfate injection USP is the FDA-approved parenteral magnesium product, supplied generically by multiple manufacturers as a 50% solution (500 mg/mL ≈ 4 mEq/mL elemental Mg) for IM injection and

as premixed dilute infusion bags (typically 1, 2, or 4 g per 100 mL) for IV use. The labeled indications include prevention and control of seizures in severe pre-eclampsia and eclampsia, treatment of torsade de pointes and life-threatening polymorphic ventricular tachycardia, and treatment of symptomatic or life-threatening hypomagnesemia [lucas1995; tzivoni1988].

Oral magnesium products are not FDA-approved drug products. They are sold as dietary supplements under the Dietary Supplement Health and Education Act (DSHEA), without pre-market FDA review of efficacy claims. Common oral salts include magnesium oxide (high elemental content per dose, low oral bioavailability, prominent cathartic effect), magnesium citrate, magnesium chloride, magnesium glycinate / bisglycinate (well-tolerated, lower GI effect at equivalent elemental dose), magnesium malate, and magnesium L-threonate [magpie2002].

Compounded Compounded Magnesium (503A)

Compounded magnesium preparations are dispensed under 503A on patient-specific prescriptions for circumstances in which a manufactured magnesium product cannot meet documented clinical need. Common 503A roles include: (1) sterile IV/IM magnesium sulfate or magnesium chloride at concentrations or volumes not commercially available (for example, custom dilutions for outpatient migraine or fibromyalgia infusion protocols, or pediatric weight-based concentrations); (2) oral magnesium blends combining specific salts at specific elemental doses that cannot be obtained from an OTC product; and (3) topical magnesium chloride preparations dispensed with explicit local-effect rationale [peikert1996].

Compounding does not duplicate the FDA-approved manufactured magnesium sulfate injection at standard strengths without a documented patient-specific reason consistent with FDA guidance on compounded copies of approved drugs [fda503a; fda_essentially_a_copy]. The OTC oral magnesium supplement market is broad; compounded oral magnesium is reserved for cases where the prescriber documents that no commercially available oral product meets the patient's clinical need.

Patient and clinician expectations should be set honestly: the established evidence base for magnesium therapy is generated with manufactured magnesium sulfate injection and with OTC oral salts [kew2014]. Compounded preparations are not separately efficacy-tested; PK and PD characteristics of a compounded preparation may differ from the reference product if concentration, excipient profile, or container closure differ. Topical magnesium for systemic effect is not supported by published absorption data and should not be framed as equivalent to oral or parenteral routes [magpie2002; mori2019].

Compounded Magnesium Formulations and Routes

Form	Concentration	Description
Magnesium sulfate injection (compounded sterile)	Custom, typically 100 mg/mL (10%), 200 mg/mL (20%), or 500 mg/mL (50%) magnesium sulfate, or 1-4 g in 100 mL diluent for IV infusion	Sterile parenteral magnesium sulfate prepared per USP <797> on patient-specific prescription, dispensed when a strength or volume not commercially available is clinically required.
Magnesium chloride injection (compounded sterile)	Custom, typically 200 mg/mL (1 g elemental Mg per 2 mL) for IM or for dilute IV infusion	Sterile parenteral magnesium chloride for outpatient infusion protocols where chloride is preferred over sulfate, or for patients with sulfate sensitivity. Prepared per USP <797>.
Oral magnesium capsule or powder (compounded)	Custom elemental magnesium per dose unit, single salt or blend	Oral magnesium prepared per USP <795> for nonsterile dosage forms. Salt selection (citrate, oxide, glycinate, malate, threonate) and elemental dose customized per prescription. Compounded oral magnesium is dispensed only when no commercially available OTC product meets the patient's documented need.
Topical magnesium chloride solution or cream (compounded)	Custom, magnesium chloride 25-40% solution or compounded into cream base	Topical magnesium dispensed with explicit local-effect rationale documented by the prescriber. Systemic absorption is not established and the preparation is not intended for systemic magnesium repletion.
Manufactured magnesium sulfate injection USP (reference product)	50% solution (500 mg/mL) for IM; premixed 1, 2, or 4 g per 100 mL for IV	FDA-approved generic injectable magnesium sulfate from multiple manufacturers, used for eclampsia, torsade de pointes, and hypomagnesemia per labeled indications.
OTC oral magnesium supplements (reference)	Variable per product, typically 100-500 mg elemental magnesium per dose unit	Dietary supplements regulated under DSHEA, not FDA-approved drug products. Common salts: oxide, citrate, chloride, glycinate (bisglycinate), malate, L-threonate.

Routes used in published literature: intravenous, intramuscular, oral, topical, transdermal.

Compounded Magnesium Dosing

Route	Population	Range	Duration	Study type
Intravenous	Severe pre-eclampsia / eclampsia, Pritchard or Zuspan obstetric regimen	Loading: 4-6 g IV over 15-20 minutes (Pritchard adds 10 g IM split between buttocks). Maintenance: 1-2 g/hour IV infusion. Continue 24 hours post-delivery or post-last-seizure.	Typically 24 hours post-delivery	FDA-approved labeled regimen; RCT-supported (Magpie 2002; Lucas 1995)
Intravenous	Torsade de pointes / polymorphic VT	1-2 g IV bolus over 1-2 minutes; may repeat once. Follow with 1-2 g/hour infusion for recurrent episodes.	Until arrhythmia controlled and underlying QT-prolonging cause addressed	FDA-approved labeled use; ACLS protocol; RCT-supported (Tzivoni 1988)
Intravenous	Symptomatic hypomagnesemia	Moderate deficit: 1-2 g IV magnesium sulfate over 30-60 minutes. Severe deficit: 4-6 g IV over 8-24 hours, may repeat per serum monitoring and renal function.	Until serum magnesium normalized and intracellular repletion plausibly complete (typically several days)	FDA-approved labeled use
Intravenous	Acute severe asthma in adults refractory to first-line therapy	2 g IV magnesium sulfate over 20 minutes as single dose adjunct to inhaled β2-agonists, ipratropium, and systemic corticosteroids	Single dose	Well-studied; Cochrane review (Kew 2014), 3Mg trial (Goodacre 2014)
Intravenous	Acute severe asthma in children refractory to first-line therapy	25-50 mg/kg IV magnesium sulfate (max 2 g) over 20 minutes	Single dose	Well-studied; Cochrane review (Griffiths 2016); MAGNETIC trial of nebulized magnesium (Powell 2013)
Intravenous	Acute migraine attack	1 g magnesium sulfate IV over 15 minutes as second-line therapy	Single dose; may repeat per protocol	Small RCT (Demirkaya 2001);

Route	Population	Range	Duration	Study type
				pilot study (Mauskop 1995)
Oral	Migraine prophylaxis	400-600 mg elemental magnesium daily (typically as citrate, dicitrate, or glycinate)	Continuous; effect assessed at 3 months	RCT (Peikert 1996); review (Domitrz 2022)
Oral	Chronic constipation	1.5 g magnesium oxide daily (approximately 900 mg elemental magnesium), or magnesium citrate equivalent	Continuous as needed; dose-limited by diarrhea	Randomized double-blind placebo-controlled trial (Mori 2019)
Oral	Mild-to-moderate depression, adjunctive supplementation	248 mg elemental magnesium daily (magnesium chloride) per Tarleton et al.	6 weeks in the published trial	Randomized open-label crossover trial (Tarleton 2017)
Oral	Mild hypertension, adjunctive	Approximately 365-450 mg elemental magnesium daily per meta-analysis median	Continuous; effect over weeks to months	Meta-analysis of randomized double-blind placebo-controlled trials (Zhang 2016)
Oral	General magnesium repletion / dietary insufficiency	Adult RDA: 400-420 mg/day (men), 310-320 mg/day (women); upper tolerable limit from supplements 350 mg/day elemental	Continuous dietary or supplemental	Dietary reference intake (NHANES analysis: Rosanoff 2012)

Doctor-prescribed for the parenteral indications (eclampsia, torsade de pointes, symptomatic hypomagnesemia, severe asthma) [tzivoni1988]. Pre-eclampsia and eclampsia dosing follows the Pritchard or Zuspan obstetric protocols and requires monitoring of deep tendon reflexes, respiratory rate, and urine output; magnesium toxicity progresses through loss of patellar reflex (serum Mg approximately 4-5 mmol/L), respiratory depression (5-6.5 mmol/L), and cardiac conduction effects at higher levels. Calcium gluconate 1 g IV is the antidote for magnesium toxicity.

Oral magnesium dosing is generally dose-limited by diarrhea, the universal upper-end side effect of all oral magnesium salts at high doses. Magnesium oxide produces the most osmotic diarrhea at equivalent elemental dose; glycinate and citrate are generally better tolerated [mori2019]. Patients with reduced renal function require dose reduction because magnesium is renally excreted; serum magnesium can accumulate to clinically dangerous levels in oliguric or anuric patients. Magnesium L-threonate is dosed by the original

developer's regimen at 1,500-2,000 mg of the threonate salt daily (delivering approximately 100-144 mg elemental magnesium), although evidence for cognitive benefit at any dose in humans is sparse [magpie2002; slutsky2010].

Compounded Magnesium Safety

Parenteral magnesium safety is dominated by dose-related neuromuscular and cardiovascular effects: loss of deep tendon reflexes at serum Mg approximately 4-5 mmol/L, respiratory depression at 5-6.5 mmol/L, and cardiac conduction abnormalities and cardiac arrest at higher levels. In the Magpie Trial [1], respiratory depression occurred in 1% of magnesium-treated women, and 0.5% had cardiac arrest, with no excess maternal mortality vs placebo. The antidote for magnesium toxicity is calcium gluconate 1 g IV. Routine monitoring during obstetric infusion includes deep tendon reflexes, respiratory rate, and urine output; serum magnesium monitoring is appropriate when toxicity is suspected or when renal function is impaired.

Oral magnesium safety in adults with normal renal function is dominated by gastrointestinal effects, diarrhea, abdominal cramping, nausea, which are dose-related and salt-specific (oxide produces the most osmotic diarrhea). Hypermagnesemia from oral magnesium is rare in patients with normal renal function but can occur with chronic high-dose supplementation, in patients with reduced creatinine clearance, and in patients receiving oral magnesium-containing laxatives or antacids without monitoring. Hypermagnesemia presents as nausea, flushing, hypotension, weakness, and at higher levels respiratory and cardiac depression [28][31].

Topical magnesium safety is largely limited to local skin irritation. Compounded preparations should specify the intended local effect; systemic-absorption claims are not well-supported. Magnesium L-threonate safety in long-term human use has not been extensively characterized; the preclinical work [21] does not substitute for systematic safety data.

Contraindications

Parenteral magnesium is contraindicated in heart block (in the absence of pacing), and is used with caution in any condition that impairs renal magnesium excretion. Concomitant aminoglycoside antibiotics potentiate neuromuscular blockade and respiratory depression risk. In pregnant patients, magnesium sulfate crosses the placenta; neonatal hypotonia and respiratory depression can occur with prolonged maternal infusion at delivery.

Oral magnesium products are contraindicated or used with caution in severe renal impairment (creatinine clearance <30 mL/min) because of accumulation risk. Magnesium-containing antacids and laxatives should be avoided in patients with reduced renal function. Patients with myasthenia gravis should not receive parenteral magnesium because of neuromuscular-junction effects [28][1].

Drug interactions

Parenteral magnesium potentiates the neuromuscular-blocking effect of non-depolarizing muscle relaxants and the respiratory-depressant effect of aminoglycoside antibiotics [31]. Concurrent calcium channel blockers may produce additive hypotension. Oral magnesium-containing antacids and supplements form non-absorbable chelates with tetracyclines, fluoroquinolones, and bisphosphonates, reducing the absorption of these drugs; doses should be separated by 2-4 hours.

Oral magnesium can reduce levothyroxine absorption and interact with digoxin handling. Magnesium is renally cleared and accumulates with thiazide and loop diuretic-induced renal wasting offset only when intake is adequate; proton pump inhibitors at long-term high doses are an established cause of clinically significant hypomagnesemia [28] [31].

Adverse events

Parenteral magnesium sulfate produces transient flushing, warmth, and a sensation of heat with bolus IV administration [28]. Dose-related effects include loss of deep tendon reflexes, weakness, respiratory depression, and at toxic levels cardiac conduction abnormalities and arrest [1]. In the Magpie Trial, adverse events leading to study-drug discontinuation occurred in 5% of magnesium-treated women vs 0.5% placebo, dominated by injection-site reactions, sweating, weakness, and respiratory effects.

Oral magnesium adverse events are dominated by dose-related diarrhea, abdominal cramping, and nausea. In the Mori et al. trial of magnesium oxide for constipation [27], adverse events were largely the expected GI effects and were dose-titratable. Topical magnesium can produce local skin irritation, particularly at high chloride concentrations [28]. Hypermagnesemia is rare in patients with normal renal function but can develop in renal impairment, with chronic high-dose oral use, or with concurrent magnesium-containing antacids.

↗ Monitoring Compounded Magnesium Therapy

Parenteral magnesium therapy in obstetrics is monitored clinically, deep tendon reflexes (loss precedes respiratory depression), respiratory rate, urine output, and level of consciousness. Serum magnesium is checked when toxicity is suspected, when renal function is impaired, or in protracted infusion [magpie2002]. Therapeutic serum range for eclampsia prophylaxis is approximately 2.0-3.5 mmol/L (4.8-8.4 mg/dL); reflexes are lost above approximately 4-5 mmol/L.

Oral magnesium supplementation does not generally require routine monitoring in adults with normal renal function. Patients with chronic kidney disease, those on chronic high-dose supplementation, and those receiving magnesium-containing antacids or laxatives in the setting of reduced renal function should have periodic serum magnesium and renal function checks. Serum magnesium is an imperfect surrogate for intracellular and total-body status [workinger2018]; ionized magnesium or red-blood-cell magnesium are research-grade alternatives but are not standard clinical assays [magpie2002].

Compounded Magnesium in Special Populations

Compounded Magnesium Evidence Quality

Evidence supporting the FDA-approved parenteral indications is strong. The Magpie Trial [magpie2002] (N=10,141 randomized) established magnesium sulfate as the standard of care for pre-eclampsia and eclampsia, supported by Lucas et al. [lucas1995] (vs phenytoin) and Belfort et al. [belfort2003] (vs nimodipine). The torsade de pointes indication rests on the Tzivoni et al. [tzivoni1988] case-series demonstration and decades of subsequent clinical experience. The acute severe asthma adjunct use is supported by the Kew et al. Cochrane review [kew2014], the 3Mg trial [goodacre2014], the MAGNETIC pediatric trial [powell2013], and the Griffiths and Kew pediatric Cochrane review [griffiths2016].

Evidence supporting oral magnesium for migraine prophylaxis is at the well-studied tier, the Peikert et al. [peikert1996] RCT, Facchinetti et al. [facchinetti1991] menstrual-migraine trial, the Mauskop and Altura [mauskop1998] and Domitrz and Cegielska [domitrz2022] reviews, and AAN/AHS Level B guidance. Magnesium for chronic constipation is supported by Mori et al. [mori2019] and long-standing clinical experience. Magnesium for blood pressure reduction is supported by the Zhang et al. meta-analysis [zhang2016] showing a modest effect size.

Evidence for depression, anxiety, and sleep is emerging at best. The Tarleton et al. [tarleton2017] open-label crossover trial is suggestive but methodologically limited; the Eby and Eby [eby2006] case series is uncontrolled; the Serefko et al. [serefko2013] and Boyle et al. [boyle2017] reviews characterize the human literature as preliminary. Magnesium L-threonate brain-penetration and cognitive-benefit claims rest on the Slutsky et al. [slutsky2010] preclinical mouse data and are not established in human RCTs; this is a preclinical-tier indication. Transdermal magnesium absorption is not well-documented; topical preparations should be framed for local effect only.

Compounded magnesium preparations are not separately efficacy-tested. The compounding role is restricted to circumstances in which a manufactured magnesium product or an OTC oral supplement cannot meet documented patient-specific need: custom IV/IM concentrations, oral salt blends not commercially available, or topical formulations with explicit local-effect rationale. The published evidence base for magnesium therapy is generated with manufactured magnesium sulfate injection and with OTC oral salts and does not transfer to compounded preparations without separate stability and tolerability evaluation.

Major Compounded Magnesium Clinical Studies

Study	Design	Participants	Duration	Finding
Magpie Trial (Magpie Trial Collaborative Group 2002, Lancet)	International randomized double-blind placebo-controlled trial of magnesium sulfate in women with pre-eclampsia	10141	Drug given until 24 hours post-delivery or post-randomization; follow-up to discharge plus 6 weeks	Magnesium sulfate reduced eclampsia by 58% (RR 0.42; 95% CI 0.29-0.60); 11 women treated to prevent one case of eclampsia [magpie2002]. No clear effect on maternal mortality. Safety acceptable with monitoring.
Lucas et al. (1995, NEJM)	Randomized trial of magnesium sulfate vs phenytoin for prevention of eclampsia in women with hypertensive disease of pregnancy	2138	Antepartum and intrapartum	Magnesium sulfate superior to phenytoin for prevention of eclampsia (0 vs 10 eclamptic convulsions; p=0.004) [lucas1995]. Established magnesium as the agent of choice over phenytoin.
Belfort et al. (2003, NEJM)	International randomized trial of magnesium sulfate vs nimodipine for prevention of eclampsia in women with severe pre-eclampsia	1650	Antepartum through 24 hours post-partum	Magnesium sulfate superior to nimodipine for prevention of eclampsia (RR 0.33; 95% CI 0.14-0.77) [belfort2003]. Ended the calcium-channel-blocker challenge to magnesium for eclampsia prevention.
Tzivoni et al. (1988, Circulation)	Case series of intravenous magnesium sulfate for torsade de pointes	12	Acute treatment	IV magnesium sulfate bolus terminated torsade de pointes polymorphic ventricular tachycardia in all treated patients, including those with normal serum magnesium [tzivoni1988]. Established

Study	Design	Participants	Duration	Finding
				magnesium as standard therapy for the arrhythmia.
Kew et al. Cochrane review (2014, Cochrane Database Syst Rev)	Systematic review and meta-analysis of randomized trials of IV magnesium sulfate for adults with acute asthma in the emergency department	14	Pooled acute-care episodes	Single IV infusion of magnesium sulfate (1.2-2 g over 15-30 minutes) reduced hospital admission in adults with severe acute asthma not responding to first-line therapy; effect on pulmonary function modest [kew2014].
Goodacre et al. 3Mg trial (2014, Health Technol Assess)	Randomized double-blind placebo-controlled trial of IV vs nebulized vs placebo magnesium in adults with acute severe asthma	1109	Acute ED episode with 30-day follow-up	IV magnesium produced a modest improvement in physiologic endpoints vs placebo; nebulized magnesium did not [goodacre2014]. Effect on admission was small.
Powell et al. MAGNETIC trial (2013, Lancet Respir Med)	Multi-center randomized double-blind placebo-controlled trial of nebulized magnesium sulfate as adjunct to standard therapy in children with severe acute asthma	508	Acute ED episode	Nebulized magnesium sulfate improved asthma severity score modestly in children with severe acute asthma vs placebo [powell2013]. Supports adjunctive use; effect size is small.
Griffiths and Kew Cochrane review (2016, Cochrane Database Syst Rev)	Systematic review and meta-analysis of IV magnesium sulfate for children with acute asthma in the emergency department	5	Pooled acute-care episodes	IV magnesium sulfate improved respiratory function and reduced hospital admission in children with severe acute asthma not responding to standard therapy [griffiths2016].
Peikert et al. (1996, Cephalalgia)	Prospective multicenter placebo-	81	12 weeks	Migraine attack frequency reduced by 41.6% on

Study	Design	Participants	Duration	Finding
	controlled double-blind randomized trial of oral magnesium dicitrate 600 mg daily for migraine prophylaxis			magnesium vs 15.8% on placebo; days with migraine and pain severity also reduced. Established oral magnesium as a Level B prophylactic [peikert1996].
Facchinetti et al. (1991, Headache)	Randomized placebo-controlled trial of oral magnesium pyrrolidone carboxylic acid 360 mg elemental daily in women with menstrual migraine	20	Two menstrual cycles	Magnesium reduced number of days with headache and pain intensity in menstrual migraine; intracellular magnesium increased in responders [facchinetti1991].
Demirkaya et al. (2001, Headache)	Randomized placebo-controlled trial of IV magnesium sulfate 1 g for acute migraine attacks	30	Acute treatment plus 24-hour follow-up	IV magnesium reduced acute migraine pain and associated symptoms (nausea, photophobia, phonophobia) vs placebo at 30, 60, and 120 minutes [demirkaya2001].
Mauskop et al. (1995, Clin Sci)	Pilot study of IV magnesium sulfate 1 g in acute migraine, stratified by serum ionized magnesium	40	Acute treatment	IV magnesium produced complete relief in 80% of patients with low serum ionized magnesium and 38% of those with normal levels; established the link between ionized magnesium and acute responsiveness [mauskop1995].
Burgess et al. (2006, Eur Heart J)	Meta-analysis of interventions (including prophylactic magnesium) for post-	8	Pooled perioperative period	Prophylactic magnesium reduced post-operative atrial fibrillation incidence in the pooled estimate [burgess2006]. Subsequent 2013 update

Study	Design	Participants	Duration	Finding
	cardiac-surgery atrial fibrillation			(Cook et al.) reported no effect, leaving practice mixed.
Cook et al. (2013, Ann Thorac Surg)	Updated meta-analysis of prophylactic magnesium for post-cardiac-surgery atrial fibrillation	22	Pooled perioperative period	Prophylactic magnesium did not reduce post-cardiac-surgery atrial fibrillation in the pooled analysis; contradicted earlier Burgess et al [cook2013]. meta-analysis conclusion.
Chiuve et al. (2011, Am J Clin Nutr)	Prospective cohort study of plasma and dietary magnesium and risk of sudden cardiac death in women (Nurses' Health Study)	88,375 women baseline	26 years follow-up	Higher plasma and dietary magnesium associated with lower risk of sudden cardiac death [chiuve2011]. Supports observational link between magnesium status and cardiovascular outcomes.
Rosanoff et al. (2012, Nutr Rev)	NHANES-based analytical review of U.S. magnesium intake and population status	—	NHANES 2005-2006 dataset	Approximately half of U.S. adults consume less than the Estimated Average Requirement for magnesium; intake especially low in older adults and in low-fruit-vegetable consumers [rosanoff2012].
Slutsky et al. (2010, Neuron)	Preclinical study of oral magnesium L-threonate in rats and aged mice	—	Up to 1 month dosing	Magnesium L-threonate increased CSF magnesium and enhanced learning and memory in aged mice [slutsky2010]. Basis for commercial threonate supplements marketed for cognitive benefit. Human RCT

Study	Design	Participants	Duration	Finding
				evidence remains sparse, preclinical only.
Tarleton et al. (2017, PLoS One)	Randomized open-label crossover trial of magnesium chloride 248 mg elemental daily in adults with mild-to-moderate depression	126	6 weeks treatment, 6 weeks control	Magnesium chloride reduced PHQ-9 depression scores by a clinically meaningful margin vs control phase [tarleton2017]. Open-label design limits inference; supports further controlled investigation.
Boyle et al. (2017, Nutrients)	Systematic review of 18 studies of magnesium supplementation for subjective anxiety and stress	—	Pooled across heterogeneous trial durations	Existing evidence is suggestive of benefit in anxiety-prone subpopulations but limited by trial quality; conclusions provisional [boyle2017].
Zhang et al. (2016, Hypertension)	Meta-analysis of 34 randomized double-blind placebo-controlled trials of oral magnesium supplementation on blood pressure	2,028 participants pooled	Median 3 months	Median 368 mg/day elemental magnesium reduced systolic BP by approximately 2 mmHg and diastolic by approximately 1.8 mmHg; effect modest but additive [zhang2016].
Mori et al. (2019, J Neurogastroenterol Motil)	Randomized double-blind placebo-controlled trial of oral magnesium oxide 1.5 g/day for chronic constipation	34	4 weeks	Magnesium oxide improved bowel-movement frequency and stool form vs placebo with expected mild osmotic-diarrhea adverse events [mori2019].
Nowak et al. (1984, Nature)	Patch-clamp electrophysiology study of mouse central neurons	—	—	Extracellular Mg^{2+} produces voltage-dependent block of glutamate-activated NMDA channels; relieved

Study	Design	Participants	Duration	Finding
				by depolarization [nowak1984]. Foundational neurophysiology paper for the magnesium-NMDA coincidence-detector framework.
Mayer et al. (1984, Nature)	Patch-clamp electrophysiology study of spinal cord neurons	—	—	Voltage-dependent Mg^{2+} block of NMDA-receptor responses in spinal cord neurons; companion finding to Nowak et al [mayer1984]. establishing the magnesium-NMDA gating mechanism.

Compounded Magnesium Pharmacokinetics & Pharmacodynamics

Pharmacokinetics

Parenteral magnesium sulfate produces immediate elevation in serum magnesium; IV bolus 1-2 g raises serum Mg by approximately 1.0-1.5 mmol/L transiently. Continuous infusion at 1-2 g/hour achieves steady-state serum magnesium in the therapeutic eclampsia-prophylaxis range (2.0-3.5 mmol/L; 4.8-8.4 mg/dL). Elimination is renal, magnesium is freely filtered and reabsorbed in the thick ascending limb and distal convoluted tubule under fine hormonal control. Half-life in patients with normal renal function is approximately 4-6 hours after infusion termination [debaaij2015].

Oral magnesium bioavailability is salt-dependent and intake-dependent. Approximate fractional absorption: magnesium oxide 4-5%, citrate 16-25%, chloride 12%, glycinate 20-25%, malate 20%. Absorption decreases at higher single doses (saturable transcellular pathway); divided dosing improves total absorption. Threonate-salt bioavailability is approximated by total magnesium content with the Slutsky et al. [slutsky2010] preclinical CSF-elevation finding not yet replicated in human plasma or CSF studies at scale. Topical magnesium absorption through intact skin is poorly characterized; the preparation is not reliably equivalent to oral or parenteral magnesium for systemic effect.

Pharmacodynamics

Pharmacodynamic effects vary by exposure level. At physiologic serum magnesium, the principal effects are cofactor function for ATP-dependent enzymes and tonic NMDA-receptor block. At supraphysiologic levels achieved with IV infusion (2-3.5 mmol/L), magnesium produces anticonvulsant, vasodilatory, and

bronchial smooth-muscle relaxant effects [tzivoni1988] [zhang2016; mori2019]. At toxic levels (>4 mmol/L), neuromuscular blockade, respiratory depression, and cardiac conduction effects emerge progressively [magpie2002].

Clinical pharmacodynamic endpoints include incidence of eclamptic convulsion (Magpie endpoint), termination of torsade de pointes (Tzivoni endpoint), reduction in hospital admission for acute severe asthma (Kew endpoint), reduction in monthly migraine attack frequency (Peikert endpoint), reduction in PHQ-9 score (Tarleton endpoint), reduction in blood pressure (Zhang endpoint), and improvement in bowel-movement frequency (Mori endpoint) [kew2014; peikert1996; tarleton2017].

↓↑ Comparing Compounded Magnesium Formulations

Among parenteral preparations, magnesium sulfate is the dominant FDA-approved injectable salt for the obstetric and antiarrhythmic indications. Magnesium chloride is occasionally compounded for IV use when sulfate is not preferred or when chloride balance is clinically relevant. The two salts differ in anion handling but produce equivalent elemental magnesium effects at matched dose [grober2015].

Among oral salts, magnesium oxide carries the highest elemental magnesium per gram of salt (60.3%) but has low fractional absorption (~4-5%) and produces the most osmotic diarrhea. Magnesium citrate (16.2% elemental) and magnesium chloride (12% elemental) have moderate bioavailability. Magnesium glycinate (bisglycinate) and magnesium malate are best tolerated at equivalent elemental dose and are typically chosen when chronic supplementation is anticipated. Magnesium L-threonate (8.1% elemental) is marketed for cognitive benefit on preclinical data [slutsky2010] and is the highest-cost-per-elemental-mg salt in the consumer market [grober2015].

Choice of salt for compounded oral magnesium is driven by the prescriber's clinical rationale: bioavailability and GI tolerability for chronic repletion (glycinate, malate), osmotic cathartic effect (oxide, citrate), or specific patient preference. Magnesium L-threonate should be framed with explicit acknowledgement that human cognitive-benefit RCT data are not established [grober2015].

🌡 Compounded Magnesium Storage and Handling

Manufactured magnesium sulfate injection is stored at controlled room temperature (20-25°C) per labeling. Compounded sterile magnesium preparations are stored per the pharmacy's stability data and beyond-use date assignment under USP <797>; refrigerated storage is typical for multi-use preparations or extended beyond-use dating [usp_797].

Oral magnesium products are stored at controlled room temperature in tight, light-resistant containers. Hygroscopic salts (notably magnesium chloride) require moisture-protective packaging. Compounded oral preparations follow USP <795> labeling and stability requirements [usp_795].

Compounded Magnesium Compounding & Operations

503A compounding

Compounded magnesium is prepared under 503A on patient-specific prescriptions in state-licensed compounding pharmacies. RonanRx prepares sterile parenteral magnesium per USP General Chapter <797> with documented active-ingredient sourcing, gravimetric and analytical verification, sterility and endotoxin testing per the pharmacy's quality-management system, and full lot traceability. Nonsterile oral and topical preparations follow USP General Chapter <795> [usp_797; usp_795].

Beyond-use dating, ingredient identity verification, and stability assessment follow the relevant USP chapter. Each compounded batch is documented per state board of pharmacy retention rules with full traceability from API lot through dispensing. Compounded magnesium is dispensed only when the prescriber documents that a manufactured magnesium sulfate injection or a commercially available OTC oral magnesium product cannot meet the patient's specific clinical need, consistent with FDA section 503A and 'essentially a copy' guidance [fda503a; fda_essentially_a_copy].

Pharmacist review

Each prescription for compounded magnesium undergoes pharmacist review prior to dispensing. The review confirms: a documented patient-specific clinical reason that a manufactured magnesium sulfate injection or an OTC oral magnesium product is not appropriate (custom concentration, custom salt blend, excipient sensitivity, or specific local-effect rationale for topical preparations); absence of contraindications (heart block for parenteral magnesium; severe renal impairment for high-dose oral magnesium; myasthenia gravis for parenteral magnesium); renal function review with dose adjustment where indicated; and concurrent-medication review for aminoglycoside, neuromuscular blocker, calcium-channel blocker, and oral drug-absorption interactions.

RonanRx does not fill prescriptions that read as routine substitution of compounded magnesium for an available manufactured or OTC product without documented clinical rationale, consistent with FDA guidance on compounded copies of approved drugs [fda_essentially_a_copy]. Topical magnesium preparations are reviewed for explicit local-effect intent; systemic-effect claims for transdermal magnesium are flagged because the absorption evidence is weak [debaaij2015].

Quality and traceability

Active pharmaceutical ingredients are sourced from FDA-registered facilities with documented certificates of analysis. Each batch is recorded with lot numbers traceable to API source, compounding date, beyond-use date, sterility test result (for sterile preparations), endotoxin test result (for parenteral preparations), and dispensing pharmacist of record. Finished product lot records are retained per state board of pharmacy retention requirements.

Cold chain

Manufactured magnesium sulfate injection USP is stored at controlled room temperature and is not a cold-chain product. Compounded sterile magnesium preparations may be assigned refrigerated storage based on the pharmacy's stability data and beyond-use date assignment under USP <797>; in that case, refrigerated transport with temperature monitoring is used between the compounding pharmacy and the patient [usp_797; usp_795]. Compounded oral and topical magnesium preparations are stored at controlled room temperature in tight, light-resistant containers.

Frequently Asked Questions About Compounded Magnesium

Is compounded magnesium the same as the magnesium sulfate IV that hospitals use for eclampsia?

No. Manufactured magnesium sulfate injection USP is the FDA-approved generic injectable used in obstetrics and emergency medicine. Compounded magnesium is pharmacy-prepared on a patient-specific prescription, typically at a strength or in a salt that is not commercially available [magpie2002]. Compounded drugs are not FDA-approved [fda503a].

Which oral magnesium salt is best?

It depends on the goal. For chronic repletion with minimal GI side effects, magnesium glycinate or malate are typically best tolerated. For osmotic cathartic effect (constipation, bowel prep), magnesium oxide or citrate are preferred [mori2019]. Magnesium citrate is well-absorbed and balances bioavailability and tolerability. Magnesium L-threonate is marketed for brain health, but human evidence is limited and the cognitive-benefit claims rest on preclinical mouse data [grober2015; slutsky2010].

Does magnesium L-threonate actually cross the blood-brain barrier?

In aged mice (Slutsky et al., 2010), oral magnesium L-threonate elevated cerebrospinal fluid magnesium and improved learning and memory [slutsky2010]. Whether the same effect occurs reliably in humans, and whether it produces cognitive benefit, is not established by published RCTs at scale. The brain-penetration claim should be framed as preclinical only.

How much weight loss should I expect from magnesium for blood pressure or migraine?

Magnesium is not a weight-loss agent. For blood pressure, the Zhang meta-analysis reported modest reductions of approximately 2 mmHg systolic and 1.8 mmHg diastolic with median 368 mg elemental daily over 3 months [zhang2016]. For migraine prophylaxis, Peikert reported a 41.6% reduction in attack frequency with 600 mg elemental daily over 12 weeks vs 15.8% on placebo [peikert1996].

Is transdermal magnesium oil effective for muscle pain or systemic supplementation?

The evidence for meaningful systemic absorption of magnesium through intact skin is weak. Topical magnesium chloride preparations may have a local effect on the skin, but they should not be relied on as equivalent to oral or parenteral magnesium for systemic repletion. Compounded topical magnesium is dispensed only with explicit local-effect rationale [grober2015].

What are the most common side effects of oral magnesium?

Diarrhea, abdominal cramping, and nausea, all dose-related and salt-dependent. Magnesium oxide produces the most osmotic diarrhea at equivalent elemental dose; glycinate and citrate are typically better tolerated [mori2019; debaaij2015]. Hypermagnesemia from oral supplementation is rare in patients with normal renal function but can occur with reduced renal clearance.

Who should not take magnesium?

Parenteral magnesium is contraindicated in heart block (without pacing) and used with caution in myasthenia gravis and renal impairment. High-dose oral magnesium should be avoided in moderate-to-severe renal impairment because of hypermagnesemia accumulation risk. Patients on aminoglycoside antibiotics or non-depolarizing neuromuscular blockers should not receive parenteral magnesium without specialist supervision [debaaij2015; magpie2002].

Does RonanRx sell compounded magnesium directly to patients?

No. Compounded magnesium requires a patient-specific prescription written by a licensed doctor for an identified patient with a documented clinical reason that a manufactured magnesium product or an OTC oral magnesium supplement 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 Magnesium

Compounded Compounded Magnesium 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

PATIENT WITH A DOCTOR

Receive your prescription

If your doctor has prescribed Compounded Magnesium, 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

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

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 and 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)

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)