CHOLINE MAGNESIUM TRISALICYLATE

THERAPEUTICS

Brands
- Trilisate

Generic?
Yes

Class
- Nonsteroidal anti-inflammatory (NSAID)

Commonly Prescribed For
(FDA approved in bold)
- Rheumatoid arthritis
- Osteoarthritis
- Other arthritis
- Acute painful shoulder
- Headaches, arthritis, painful inflammatory disorders
- Musculoskeletal pain

How the Drug Works
- Choline magnesium trisalicylate (CMT) is a nonacetylated salicylate. Like other NSAIDs, inhibits cyclo-oxygenase thus inhibiting synthesis of prostaglandins, mediators of inflammation

How Long until It Works
- Roughly 0.5–2 hours

If It Works
- Continue to use

If It Doesn’t Work
- Some patients only have a partial response where some symptoms are improved but others persist or continue to wax and wane without stabilization of pain
- Other patients may be nonresponders, sometimes called treatment-resistant or treatment-refractory
- Consider increasing dose, switching to another agent or route, adding an appropriate augmenting agent, or utilizing an entirely different nonpharmacologic approach (e.g. neuromodulation)
- Consider biofeedback or hypnosis for pain
- Consider physical medicine approaches to pain relief

- Consider the presence of noncompliance and counsel patient
- Switch to another agent with fewer adverse effects
- Consider evaluation for another diagnosis or for a comorbid condition (e.g. medical illness, substance abuse, etc.)

Best Augmenting Combos for Partial Response or Treatment Resistance
- Consider adding an opioid

Tests
- None for healthy individuals
- BUN/creatinine – if suspected renal issues
- Consider checking liver function tests for long-term use

ADVERSE EFFECTS (AEs)

How Drug Causes AEs
- Effects on prostaglandins likely cause most GI and renal AEs

Notable AEs
- Inhibition of platelet aggregation is usually mild
- Elevation in hepatic transaminases (usually borderline)
- GI: diarrhea, dyspepsia, abdominal pain
- Edema
- Dizziness, headache, fatigue, insomnia, nervousness, somnolence
- Pruritus, rash
- Constipation, flatulence, guaiac positive, nausea, gastritis, stomatitis, vomiting, xerostomia, tinnitus

Life-Threatening or Dangerous AEs
- GI ulcers and bleeding, increasing with duration of therapy
- May worsen congestive heart failure
- May increase risk of fluid retention and edema, cardiovascular events, including MI and stroke
- Renal insufficiency, proteinuria, and hyperkalemia
- Thrombocytopenia
- Hypersensitivity reactions: most common in patients with asthma, anaphylactoid reaction, Stevens–Johnson syndrome, toxic epidermal necrolysis
Weight Gain
- Unusual

Sedation
- Not unusual

What to Do about AEs
- For significant GI or intracranial bleeding, stop drug. Some AEs respond to lowering dose
- Administer tablet with food or milk to GI distress
- For GI irritation, consider sucralfate, H₂-receptor antagonist, proton pump inhibitors, or prostaglandin analog

Best Augmenting Agents for AEs
- Proton pump inhibitors may reduce risk of GI ulcers
- Many AEs cannot be improved with an augmenting agent

DOSING AND USE

Usual Dosage Range
- 1–4.5 g/day

Dosage Forms
- Tablets: 500 mg, 750 mg

How to Dose
- Pain management: initial dose 500 mg twice daily, increase to 1500 mg 3 times daily as appropriate
- Geriatric: usual dose 1 750 mg tablet 3 times daily

Dosing Tips
- Taking with food decreases absorption and reduces GI AEs

Overdose
- GI distress or bleed, drowsiness, paresthesias, and numbness are most common. Severe overdose may cause hypertension, metabolic acidosis, hepatic or renal failure, and cardiac arrest. Consider multiple doses of activated charcoal or hemodialysis for severe cases

Long-Term Use
- Safe for long-term use

Habit Forming
- No

How to Stop
- No need to taper

Pharmacokinetics
- Half-life varies with the amount administered. Low dose half-life is 2–3 hours; and half-life with high dose is 30 hours, dose peak at ~2 hours. Minimal hepatic metabolism. Predominant renal excretion 60% urine and fecal 33%. 90% protein bound

Drug Interactions
- Use with alcohol, bisphosphonates, corticosteroids, anticoagulants, and other NSAIDs increases GI bleeding risk
- Cyclosporine and NSAIDs increase risk of nephrotoxicity
- Cholestyramine may decrease absorption
- Aspirin use may decrease NSAID serum levels and increases risk of GI AEs
- May blunt effectiveness of beta-blockers and angiotensin-converting enzyme (ACE) inhibitors
- May decrease effect of loop diuretics and spironolactone
- May increase drug levels and effects of digoxin, aminoglycosides, methotrexate, lithium, and phenytoin

Other Warnings/Precautions
- Risk factors for GI bleeding include smoking, alcoholism, older age, poor health status, and treatment with anticoagulants or corticosteroids
- May cause photosensitivity

Do Not Use
- Hypersensitivity to any NSAID, treatment with anticoagulants, renal or hepatic disease, age under 12, rectal bleeding or proctitis (suppositories), pain in the setting of coronary artery bypass graft (CABG) surgery
SPECIAL POPULATIONS

Renal Impairment
- Use with caution in chronic renal insufficiency as may worsen renal function. Use low dose and monitor frequently.

Hepatic Impairment
- Use with caution in patients with significant disease. May have increased risk of GI bleeding and toxicity.

Cardiac Impairment
- May cause fluid retention and decompensation in patients with cardiac failure. May cause hypertension or lower effectiveness of antihypertensives.

Elderly
- More likely to experience GI bleeding or CNS AEs.

Pregnancy
- Category C, except category D in 3rd trimester. May prolong pregnancy and increase risk of septal heart defects, incidence of dystocia, and delivery time. May cause premature closure of ductus arteriosus and pulmonary hypertension. Do not use, especially in 3rd trimester.

Breast-Feeding
- Most NSAIDs are excreted in breast milk. Do not breast-feed due to effects on infant cardiovascular system.

THE ART OF PAIN PHARMACOLOGY

Potential Advantages
- Can use once-daily dosing
- Less apt to result in excessive bleeding/GI bleeding

Potential Disadvantages
- Usual NSAID drawbacks

Primary Target Symptoms
- Pain
- Inflammation

Pearls
- Used for rheumatoid arthritis, osteoarthritis, and painful osseous metastases
- Nonacetylated salicylates like CMT have less effect on platelet function and less GI mucosal insult than traditional nonselective NSAIDs

Suggested Reading


