CHLORPROMAZINE

THERAPEUTICS

Brands
• Thorazine, Largactil

Generic?
Yes

Class
• Antiemetic, antipsychotic

Commonly Prescribed for
(FDA approved in bold)
• Antiemetic
• Intractable hiccups
• Psychosis, schizophrenia
• Mania in bipolar disorder
• Acute intermittent porphyria
• Tetanus
• Restlessness and apprehension before surgery
• Hyperactivity and behavioral problems (children)
• Migraine (acute)

How the Drug Works
• Dopamine receptor antagonist with greatest action at D2 receptors. Also has antihistamine, anticholinergic effects, and blocks alpha-adrenergic receptors

How Long Until It Works
• Migraine – 1 hour (oral) or less than 30 minutes (IV)

If It Works
• Use at lowest required dose
• Monitor QT corrected (QTc) interval

If It Doesn’t Work
• Change to another agent

Best Augmenting Combos for Partial Response or Treatment-Resistance
• For migraine, can be used with dihydroergotamine or NSAIDs

Tests
• Obtain blood pressure and pulse before initial IV and monitor QTc with ECG

ADVERSE EFFECTS (AEs)

How Drug Causes AEs
• Anticholinergic effects produce most AEs (sedation, blurred vision, dry mouth). Hypotension and dizziness are related to alpha-adrenergic blockade, and motor AEs are related to dopamine blocking effects

Notable AEs
• Akathisia, extrapyramidal symptoms, parkinsonism
• Dizziness, sedation, orthostatic hypotension, tachycardia, urinary retention, depression
• Long-term use: weight gain, glucose intolerance, sexual dysfunction, hyperprolactinemia

Life-Threatening or Dangerous AEs
• Tardive dyskinesias
• Neuroleptic malignant syndrome (rare)
• Jaundice, agranulocytosis (rare)

Weight Gain
• Common (with chronic use)

Sedation
• Problematic

What to Do About AEs
• Lowering dose or changing to another antiemetic improves most AEs
• Rarely causes ECG changes. Use with caution in patients if QTc is above 450 (females) or 440 (males) and do not administer with QTc greater than 500
• If excessive sedation, use only as a rescue agent for intractable migraine in hospitalized patients or when patients can lie down or sleep

Best Augmenting Agents for AEs
• Give fluids to avoid hypotension, tachycardia, and dizziness
• Give anticholinergics (diphenhydramine or benztropine) or benzodiazepines for extrapyramidal reactions
• Amantadine may improve motor AEs
**Dosage and Use**

**Usual Dosage Range**
- Migraine: up to 200 mg/day IV, IM, or oral in divided doses

**Dosage Forms**
- Tablets: 10 mg, 25 mg, 50 mg, 100 mg, 200 mg
- Injection: 25 mg/mL
- Liquid: 25 mg/5 mL, 100 mg/5 mL
- Suppository: 25 mg, 100 mg

**How to Dose**
- Oral: Give 10–25 mg and repeat as needed every 4–6 hours. Patients with previous exposure and few significant AEs may increase dose and use up to 200 mg/day in divided doses
- IV/IM: Give 12.5–50 mg every 4–8 hours up to 200 mg/day

**Dosing Tips**
- In hospitalized patients, start with lower dose to ensure drug is tolerated and increase as needed to effective dose
- Warn patients not to drive
- Check ECG daily while patients are treated and monitor blood pressure

**Overdose**
- CNS depression, hypotension, or extrapyramidal reactions are most common. Tachycardia, restlessness, convulsions, and respiratory depression may occur

**Long-Term Use**
- Safe for long-term use with appropriate monitoring. Tardive dyskinesias may be irreversible

**Habit Forming**
- No

**How to Stop**
- No need to taper

**Pharmacokinetics**
- Metabolized by CYP2D6. Tmax 1–4 hours and half-life 8–33 hours

**Drug Interactions**
- Use with CNS depressants (barbiturates, opiates, general anesthetics) potentiates CNS AEs
- May enhance effects of antihypertensives
- Use with alcohol or diuretics may increase hypotension
- May decrease effectiveness of dopaminergic agents
- Reduces effectiveness of anticoagulants
- May increase phenytoin levels
- The combination of lithium and neuroleptics has been reported to produce an encephalopathy similar to neuroleptic malignant syndrome

**Other Warnings/Precautions**
- Neuroleptic malignant syndrome is characterized by fever, rigidity, confusion, and autonomic instability, and is most common with IV typical neuroleptics such as chlorpromazine
- Hypersensitivity to drug, CNS depression or QTc greater than 500

**Special Populations**

**Renal Impairment**
- No known effects

**Hepatic Impairment**
- No known effects

**Cardiac Impairment**
- May worsen orthostatic hypotension

**Elderly**
- More sensitive to CNS AEs, use lower doses

**Children and Adolescents**
- Appears safe in children over age 1, but mostly used for behavioral problems. Not a first line agent in pediatric migraine
Pregnancy
• Category C. Use only if benefit outweighs risks

Breast Feeding
• Some drug is found in breast milk and may cause sedation or movement problems in infants. Do not use for migraine

THE ART OF NEUROPHARMACOLOGY

Potential Advantages
• Effective drug for severe migraine. Sedation may be helpful for some patients and akathisia may be less common than with other antiemetics

Potential Disadvantages
• Significant AEs including extrapyramidal reactions, sedation, and hypotension.

Primary Target Symptoms
• Headache, nausea

Pearls
• Effective in refractory migraine and status migrainosus. Often combined with dihydroergotamine, given about 30 minutes after chlorpromazine
• Pretreat or combine with diphenydramine, 25–50 mg, to reduce rate of akathisia and dystonic reactions
• Generally used as a “rescue” treatment in severe migraine when first-line medications (triptans, dihydroergotamine, NSAIDs) have failed

Suggested Reading