### CHLORPROMAZINE

<table>
<thead>
<tr>
<th>THERAPEUTICS</th>
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<tbody>
<tr>
<td><strong>Brands</strong></td>
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<tr>
<td>• Thorazine</td>
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<tr>
<td><em>see index for additional brand names</em></td>
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<tr>
<td><strong>Generic?</strong></td>
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<tr>
<td>Yes</td>
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<tr>
<td><strong>Class</strong></td>
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<tr>
<td>• Neuroscience-based Nomenclature: dopamine and serotonin receptor antagonist (DS-RAn)</td>
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<tr>
<td>• Conventional antipsychotic (neuroleptic, phenothiazine, dopamine 2 antagonist, antiemetic)</td>
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<tr>
<td><strong>Commonly Prescribed for</strong></td>
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<tr>
<td><em>(bold for FDA approved)</em></td>
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<tr>
<td>• Schizophrenia</td>
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<td>• Nausea, vomiting</td>
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<tr>
<td>• Restlessness and apprehension before surgery</td>
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<tr>
<td>• Acute intermittent porphyria</td>
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<td>• Manifestations of manic type of manic-depressive illness</td>
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<tr>
<td>• Tetanus (adjunct)</td>
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<td>• Intractable hiccups</td>
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<td>• Combativeness and/or explosive hyperexcitable behavior (in children)</td>
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<td>• Hyperactive children who show excessive motor activity with accompanying conduct disorders consisting of some or all of the following symptoms: impulsivity, difficulty sustaining attention, aggressivity, mood lability, and poor frustration tolerance</td>
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<tr>
<td>• Psychosis</td>
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<td>• Bipolar disorder</td>
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<tr>
<td><strong>How the Drug Works</strong></td>
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<tr>
<td>• Blocks dopamine 2 receptors, reducing positive symptoms of psychosis and improving other behaviors</td>
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<td>• Combination of dopamine D2, histamine H1, and cholinergic M1 blockade in the vomiting center may reduce nausea and vomiting</td>
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<td><strong>How Long Until It Works</strong></td>
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<tr>
<td>• Psychotic symptoms can improve within 1 week, but it may take several weeks for full effect on behavior</td>
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<td>• Actions on nausea and vomiting are immediate</td>
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<td><strong>If It Works</strong></td>
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<tr>
<td>• Most often reduces positive symptoms in schizophrenia but does not eliminate them</td>
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<td>• Most schizophrenic patients do not have a total remission of symptoms but rather a reduction of symptoms by about a third</td>
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<tr>
<td>• Continue treatment in schizophrenia until reaching a plateau of improvement</td>
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<tr>
<td>• After reaching a satisfactory plateau, continue treatment for at least a year after first episode of psychosis in schizophrenia</td>
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<td>• For second and subsequent episodes of psychosis in schizophrenia, treatment may need to be indefinite</td>
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<tr>
<td>• Reduces symptoms of acute psychotic mania but not proven as a mood stabilizer or as an effective maintenance treatment in bipolar disorder</td>
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<tr>
<td>• After reducing acute psychotic symptoms in mania, switch to a mood stabilizer and/or an atypical antipsychotic for mood stabilization and maintenance</td>
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<td><strong>If It Doesn’t Work</strong></td>
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<tr>
<td>• Consider trying one of the first-line atypical antipsychotics (risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole, paliperidone, amisulpride, asenapine, iloperidone, lurasidone)</td>
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<tr>
<td>• Consider trying another conventional antipsychotic</td>
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<tr>
<td>• If 2 or more antipsychotic monotherapies do not work, consider clozapine</td>
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<tr>
<td><strong>Best Augmenting Combos for Partial Response or Treatment Resistance</strong></td>
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<tr>
<td>• Augmentation of conventional antipsychotics has not been systematically studied</td>
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<td>• Addition of a mood-stabilizing anticonvulsant such as valproate, carbamazepine, or lamotrigine may be helpful in both schizophrenia and bipolar mania</td>
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<td>• Augmentation with lithium in bipolar mania may be helpful</td>
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<td>• Addition of a benzodiazepine, especially short-term for agitation</td>
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<td><strong>Tests</strong></td>
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<td>• Since conventional antipsychotics are frequently associated with weight gain, before starting treatment, weigh all patients and determine if the patient is already overweight (BMI 25.0–29.9) or obese (BMI ≥30)</td>
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</table>
CHLORPROMAZINE (continued)

- Before giving a drug that can cause weight gain to an overweight or obese patient, consider determining whether the patient already has pre-diabetes (fasting plasma glucose 100–125 mg/dL), diabetes (fasting plasma glucose >126 mg/dL), or dyslipidemia (increased total cholesterol, LDL cholesterol and triglycerides; decreased HDL cholesterol), and treat or refer such patients for treatment, including nutrition and weight management, physical activity counseling, smoking cessation, and medical management
- **Monitor weight and BMI during treatment**
- **Consider monitoring fasting triglycerides monthly for several months in patients at high risk for metabolic complications and when initiating or switching antipsychotics**
- **While giving a drug to a patient who has gained >5% of initial weight, consider evaluating for the presence of pre-diabetes, diabetes, or dyslipidemia, or consider switching to a different antipsychotic**
- **Should check blood pressure in the elderly before starting and for the first few weeks of treatment**
- **Monitoring elevated prolactin levels of dubious clinical benefit**
- **Phenothiazines may cause false positive phenylketonuria results**
- **Patients with low white blood cell count (WBC) or history of drug-induced leucopenia/neutropenia should have complete blood count (CBC) monitored frequently during the first few months and chlorpromazine should be discontinued at the first sign of decline of WBC in the absence of other causative factors**

- **Antihistaminic actions may cause sedation, weight gain**
- **By blocking alpha 1 adrenergic receptors, it can cause dizziness, sedation, and hypotension**
- **Mechanism of weight gain and any possible increased incidence of diabetes or dyslipidemia with conventional antipsychotics is unknown**

**Notable Side Effects**
- Neuroleptic-induced deficit syndrome
- Akathisia
- Priapism
- Extrapyramidal symptoms, parkinsonism, tardive dyskinesia
- Galactorrhea, amenorrhea
- **Dizziness, sedation, impaired memory**
- **Dry mouth, constipation, urinary retention, blurred vision**
- **Decreased sweating**
- **Sexual dysfunction**
- **Hypotension, tachycardia, syncope**
- **Weight gain**

**Life-Threatening or Dangerous Side Effects**
- Rare neuroleptic malignant syndrome
- Rare jaundice, agranulocytosis
- Rare seizures
- Increased risk of death and cerebrovascular events in elderly patients with dementia-related psychosis

**Weight Gain**
- **Many experience and/or can be significant in amount**

**Sedation**
- **Tolerance to sedation can develop over time**

**What to Do About Side Effects**
- Wait
- Wait
- Wait
- For motor symptoms, add an anticholinergic agent
- Reduce the dose
- For sedation, give at night
One of the few antipsychotics available as a suppository. Treatment should be suspended if absolute neutrophil count falls below 1,000/mm³.

**Overdose**
- Extrapyramidal symptoms, sedation, hypotension, coma, respiratory depression.

**Long-Term Use**
- Some side effects may be irreversible (e.g., tardive dyskinesia).

**Habit Forming**
- No.

**How to Stop**
- Slow down-titration of oral formulation (over 6–8 weeks), especially when simultaneously beginning a new antipsychotic while switching (i.e., cross-titration).
- Rapid oral discontinuation may lead to rebound psychosis and worsening of symptoms.
- If antiparkinson agents are being used, they should be continued for a few weeks after chlorpromazine is discontinued.

**Pharmacokinetics**
- Half-life approximately 8–33 hours.

**Drug Interactions**
- May decrease the effects of levodopa, dopamine agonists.
- May increase the effects of antihypertensive drugs except for guanethidine, whose antihypertensive actions chlorpromazine may antagonize.
- Additive effects may occur if used with CNS depressants.
- Some pressor agents (e.g., epinephrine) may interact with chlorpromazine to lower blood pressure.
- Alcohol and diuretics may increase the risk of hypotension.
- Reduces effects of anticoagulants.
- May reduce phenytoin metabolism and increase phenytoin levels.
- Plasma levels of chlorpromazine and propranolol may increase if used concomitantly.
- Some patients taking a neuroleptic and lithium have developed an encephalopathic syndrome.

**Best Augmenting Agents for Side Effects**
- Benztropine or trihexyphenidyl for motor side effects.
- Sometimes amantadine can be helpful for motor side effects.
- Benzodiazepines may be helpful for akathisia.
- Many side effects cannot be improved with an augmenting agent.

**DOSING AND USE**

**Usual Dosage Range**
- 200–800 mg/day.

**Dosage Forms**
- Tablet 10 mg, 25 mg, 50 mg, 100 mg, 200 mg.
- Capsule 30 mg, 75 mg, 150 mg.
- Ampul 25 mg/mL; 1 mL, 2 mL.
- Vial 25 mg/mL; 10 mL.
- Liquid 10 mg/5 mL.
- Suppository 25 mg, 100 mg.

**How to Dose**
- Psychosis: increase dose until symptoms are controlled; after 2 weeks reduce to lowest effective dose.
- Psychosis (intramuscular): varies by severity of symptoms and inpatient/outpatient status.

**Dosing Tips**
- Low doses may have more sedative actions than antipsychotic actions.
- Low doses have been used to provide short-term relief of daytime agitation and anxiety and to enhance sedative hypnotic actions in nonpsychotic patients, but other treatment options such as atypical antipsychotics are now preferred.
- Higher doses may induce or worsen negative symptoms of schizophrenia.
- Ampuls and vials contain sulfites that may cause allergic reactions, particularly in patients with asthma.

**Weight loss, exercise programs, and medical management for high BMIs, diabetes dyslipidemia**
syndrome similar to neuroleptic malignant syndrome

**Other Warnings/Precautions**
- If signs of neuroleptic malignant syndrome develop, treatment should be immediately discontinued
- Use cautiously in patients with alcohol withdrawal or convulsive disorders because of possible lowering of seizure threshold
- Use with caution in patients with respiratory disorders, glaucoma, or urinary retention
- Avoid extreme heat exposure
- Avoid undue exposure to sunlight
- Antiemetic effect of chlorpromazine may mask signs of other disorders or overdose; suppression of cough reflex may cause asphyxia
- Use only with caution if at all in Parkinson’s disease or Lewy body dementia

**Do Not Use**
- If patient is in a comatose state
- If patient is taking metrizamide or large doses of CNS depressants
- If there is a proven allergy to chlorpromazine
- If there is a known sensitivity to any phenothiazine

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**SPECIAL POPULATIONS**

**Renal Impairment**
- Use with caution

**Hepatic Impairment**
- Use with caution

**Cardiac Impairment**
- Cardiovascular toxicity can occur, especially orthostatic hypotension

**Elderly**
- Lower doses should be used and patient should be monitored closely
- Often do not tolerate sedating actions of chlorpromazine
- Although conventional antipsychotics are commonly used for behavioral disturbances in dementia, no agent has been approved for treatment of elderly patients with dementia-related psychosis

**Children and Adolescents**
- Can be used cautiously in children or adolescents over age 1 with severe behavioral problems
- Oral – 0.25 mg/lb every 4–6 hours as needed; rectal – 0.5 mg/lb every 6–8 hours as needed; IM – 0.25 mg/lb every 6–8 hours as needed; maximum 40 mg/day (under 5), 75 mg/day (5–12)
- Do not use if patient shows signs of Reye’s syndrome
- Generally consider second-line after atypical antipsychotics

**Pregnancy**
- Effective June 30, 2015, the US FDA requires changes to the content and format of pregnancy and lactation information in prescription drug labels, including the elimination of the pregnancy letter categories; the Pregnancy and Lactation Labeling Rule (PLLR or final rule) applies only to prescription drugs and will be phased in gradually for drugs approved on or after June 30, 2001
- Controlled studies have not been conducted in pregnant women
- There is a risk of abnormal muscle movements and withdrawal symptoms in newborns whose mothers took an antipsychotic during the third trimester; symptoms may include agitation, abnormally increased or decreased muscle tone, tremor, sleepiness, severe difficulty breathing, and difficulty feeding
- Reports of extrapyramidal symptoms, jaundice, hyperreflexia, hyporeflexia in infants whose mothers took a phenothiazine during pregnancy
- Chlorpromazine should generally not be used during the first trimester
- Chlorpromazine should be used during pregnancy only if clearly needed
• Psychotic symptoms may worsen during pregnancy and some form of treatment may be necessary
• Atypical antipsychotics may be preferable to conventional antipsychotics or anticonvulsant mood stabilizers if treatment is required during pregnancy

Breast Feeding
• Some drug is found in mother’s breast milk
• Effects on infant have been observed (dystonia, tardive dyskinesia, sedation)

* Recommended either to discontinue drug or bottle feed

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### THE ART OF PSYCHOPHARMACOLOGY

#### Potential Advantages
- Intramuscular formulation for emergency use
- Patients who require sedation for behavioral control

#### Potential Disadvantages
- Patients with tardive dyskinesia
- Children
- Elderly
- Patients who wish to avoid sedation

#### Primary Target Symptoms
- Positive symptoms of psychosis
- Motor and autonomic hyperactivity
- Violent or aggressive behavior

#### Pearls
- Chlorpromazine is one of the earliest classical conventional antipsychotics
- Chlorpromazine has a broad spectrum of efficacy, but risk of tardive dyskinesia and

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the availability of alternative treatments make its utilization outside of psychosis a short-term and second-line treatment option

• Chlorpromazine is a low-potency phenothiazine
• Sedative actions of low-potency phenothiazines are an important aspect of their therapeutic actions in some patients and side effect profile in others
• Low-potency phenothiazines like chlorpromazine have a greater risk of cardiovascular side effects
• Patients have very similar antipsychotic responses to any conventional antipsychotic, which is different from atypical antipsychotics where antipsychotic responses of individual patients can occasionally vary greatly from one atypical antipsychotic to another
• Patients with inadequate responses to atypical antipsychotics may benefit from a trial of augmentation with a conventional antipsychotic such as chlorpromazine or from switching to a conventional antipsychotic such as chlorpromazine
• However, long-term polypharmacy with a combination of a conventional antipsychotic such as chlorpromazine with an atypical antipsychotic may combine their side effects without clearly augmenting the efficacy of either
• For treatment-resistant patients, especially those with impulsivity, aggression, violence, and self-harm, long-term polypharmacy with 2 atypical antipsychotics or with 1 atypical antipsychotic and 1 conventional antipsychotic may be useful or even necessary while closely monitoring
• In such cases, it may be beneficial to combine 1 depot antipsychotic with 1 oral antipsychotic
Suggested Reading


