

# DIPHENHYDRAMINE

## THERAPEUTICS

**Brands** • Benadryl, Sominex  
*see index for additional brand names*

**Generic?** Yes

### **Class**

- Antihistamine; anticholinergic agent

### **Commonly Prescribed for**

*(bold for FDA approved)*

- **Allergy symptoms**
- **Motion sickness**
- **Occasional sleeplessness**
- **Antiparkinsonism**
- Extrapyramidal disorders



### **How the Drug Works (for extrapyramidal disorders)**

- Diminishes the excess acetylcholine activity caused by removal of dopamine inhibition when dopamine receptors are blocked
- Also has potent histamine 1 antagonist properties

### **How Long Until It Works (for extrapyramidal disorders)**

- For extrapyramidal disorders and parkinsonism, onset of action can be within minutes or hours

### **If It Works (for extrapyramidal disorders)**

- Reduces motor side effects
- Does not lessen the ability of antipsychotics to cause tardive dyskinesia

### **If It Doesn't Work (for extrapyramidal disorders)**

- Consider switching to trihexyphenidyl, benzotropine, or a benzodiazepine
- Disorders that develop after prolonged antipsychotic use may not respond to treatment
- Consider discontinuing the agent that precipitated the EPS



### **Best Augmenting Combos for Partial Response or Treatment Resistance**

- If ineffective, switch to another agent rather than augment

- Diphenhydramine itself is an augmenting agent to antipsychotics

### **Tests**

- None for healthy individuals

## SIDE EFFECTS

### **How Drug Causes Side Effects**

- Blocking histamine 1 receptors can cause sedation
- Preventing the action of acetylcholine on muscarinic receptors can cause anticholinergic effects such as dry mouth, blurred vision, constipation

### **Notable Side Effects**

- Sedation, dizziness
- Constipation, nausea
- Dry mouth, blurred vision



### **Life-Threatening or Dangerous Side Effects**

- Rare convulsions (at high doses)
- Urinary retention
- Tachycardia, cardiac arrhythmias
- Confusion
- Paralytic ileus/bowel obstruction

### **Weight Gain**



- Frequent and can be significant in amount

### **Sedation**



- Many experience and/or can be significant in amount

### **What to Do About Side Effects**

- For confusion or hallucinations, discontinue use
- For sedation, lower the dose and/or take the entire dose at night
- For dry mouth, chew gum or drink water
- For urinary retention, obtain a urological evaluation; may need to discontinue use

### **Best Augmenting Agents for Side Effects**

- Many side effects cannot be improved with an augmenting agent

**DOSING AND USE**

**Usual Dosage Range**

- Oral: 50 mg/day
- Injection: 10–50 mg

**Dosage Forms**

- Injection 50 mg/mL
- Capsule 50 mg
- Elixir 12.5 mg/5 mL
- Also available in formulations in combination with other medications

**How to Dose**

- Injection: 10–50 mg intravenously at a rate not exceeding 25 mg/min or deep intramuscularly; can dose at 100 mg if required; maximum daily dose 400 mg



**Dosing Tips**

- If drug-induced EPS occur soon after initiation of a neuroleptic drug, they are likely to be transient; thus, attempt to withdraw diphenhydramine after 1–2 weeks to determine if still needed
- The injection should be used for parkinsonism only if oral therapy is impossible or contraindicated

**Overdose**

- CNS depression, CNS stimulation (more likely in pediatric patients), dry mouth, dilated pupils, flushing, gastrointestinal symptoms

**Long-Term Use**

- Safe
- Effectiveness may decrease over time, even after a few doses, but side effects such as cognitive impairment and sedation may persist

**Habit Forming**

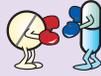
- No

**How to Stop**

- Tapering generally not necessary

**Pharmacokinetics**

- Plasma half-life approximately 8 hours; may be longer in children and in the elderly



**Drug Interactions**

- May potentiate the effects of other CNS depressants
- If anticholinergic agents are used with diphenhydramine, the anticholinergic effects may be enhanced



**Other Warnings/  
Precautions**

- Use with caution in patients with a history of bronchial asthma, lower respiratory disease, increased intraocular pressure, hyperthyroidism, cardiovascular disease, or hypertension
- May have additive effects if taken with anticholinergic agents

**Do Not Use**

- If patient is breast feeding
- In neonates or premature infants
- In patients with glaucoma, particularly angle-closure glaucoma
- In patients with pyloric or duodenal obstruction, stenosing peptic ulcers, prostate hypertrophy, or bladder neck obstructions
- If patient is taking an MAOI
- If there is a proven allergy to diphenhydramine

**SPECIAL POPULATIONS**

**Renal Impairment**

- No dose adjustment necessary

**Hepatic Impairment**

- No dose adjustment necessary

**Cardiac Impairment**

- Not systematically evaluated in patients with cardiac impairment

**Elderly**

- Some patients may tolerate lower doses better
- Diphenhydramine injection is preferred for parkinsonism in the elderly who are unable to tolerate more potent agents



### **Children and Adolescents**

- Not recommended for children under age 12
- Injection: 5 mg/kg/24 hours or 150 mg/m<sup>2</sup>/24 hours; maximum daily dose 300 mg; divide into 4 doses; can be given intravenously at a rate not exceeding 25 mg/min, or deep intramuscularly
- Contraindicated in neonates and premature infants



### **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
- Animal studies have not shown adverse effects

### **Breast Feeding**

- Contraindicated

## **THE ART OF PSYCHOPHARMACOLOGY**

### **Potential Advantages**

- Mild cases of parkinsonism

### **Potential Disadvantages**

- Can be too sedating for some patients
- Can cause confusion in elderly patients and in patients with dementia

### **Primary Target Symptoms**

- Extrapyramidal disorders



### **Pearls**

- Can be useful for occasional insomnia
- Patients with cognitive impairment may do poorly
- Can cause cognitive side effects with chronic use, so periodic trials of discontinuation may be useful to justify continuous use, especially in institutional settings when used as an adjunct to antipsychotics
- Can be abused in institutional or correctional settings



### **Suggested Reading**

Gonzalez F. Diphenhydramine may be useful as a palliative treatment for patients dying with Parkinson's disease and tremors: a case report and discussion. *Am J Hosp Palliat Care* 2010;26(6):474–5.