

BENZTROPINE

THERAPEUTICS

Brands • Cogentin
see index for additional brand names

Generic? Yes



Class

- Antiparkinson agent; anticholinergic

Commonly Prescribed for

(bold for FDA approved)

- **Extrapyramidal disorders**
- **Parkinsonism**
- Acute dystonic reactions
- Idiopathic generalized dystonia
- Focal dystonias
- Dopa-responsive dystonia



How the Drug Works

- Diminishes the excess acetylcholine activity caused by removal of dopamine inhibition when dopamine receptors are blocked
- May also inhibit the reuptake and storage of dopamine at central dopamine receptors, prolonging dopamine action

How Long Until It Works

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

If It Works

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

If It Doesn't Work

- Consider switching to trihexyphenidyl, diphenhydramine, 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
- Benztropine is itself an augmenting agent to antipsychotics

Tests

- None for healthy individuals

SIDE EFFECTS

How Drug Causes Side Effects

- Prevents the action of acetylcholine on muscarinic receptors

Notable Side Effects

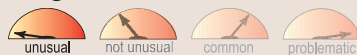
- Dry mouth, blurred vision, diplopia
- Confusion, hallucinations
- Constipation, nausea, vomiting
- Dilation of colon/paralytic ileus/bowel obstruction
- Erectile dysfunction



Life-Threatening or Dangerous Side Effects

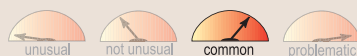
- Angle-closure glaucoma
- Heat stroke, especially in elderly patients
- Tachycardia, cardiac arrhythmias, hypotension
- Urinary retention
- Anticholinergic agents such as benztropine can exacerbate or unmask tardive dyskinesia

Weight Gain



- Reported but not expected

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

- Extrapryramidal disorders: 2–8 mg/day
- Parkinsonism: 0.5–6 mg/day

Dosage Forms

- Tablet 0.5 mg, 1 mg, 2 mg
- Injection 1 mg/mL

How to Dose

- Extrapryramidal disorders: 1–4 mg once or twice daily; can be given orally or parenterally
- Parkinsonism (oral): initial 0.5 mg once daily; increase by 0.5 mg at 5–6 day intervals until desired efficacy is reached



Dosing Tips

- If drug-induced EPS occur soon after initiation of a neuroleptic drug, they are likely to be transient; thus, attempt to withdraw benztropine after 1–2 weeks to determine if still needed
- Patients may take benztropine once daily at night to improve sleep and allow for earlier rising in the morning
- Taking benztropine with meals can reduce side effects
- Intramuscular and intravenous dosing are equally effective and fast acting

Overdose

- Circulatory collapse, cardiac arrest, respiratory depression or arrest, psychosis, shock, coma, seizure, ataxia, combativeness, anhidrosis and hyperthermia, fever, dysphagia, decreased bowel sounds, sluggish pupils

Long-Term Use

- Safe
- Effectiveness may decrease over time (years), and side effects such as sedation and cognitive impairment may worsen

Habit Forming

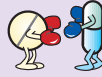
- No

How to Stop

- Taper not necessary

Pharmacokinetics

- Half-life 36 hours, although greatest effect lasts about 6–8 hours
- Metabolism is not well understood



Drug Interactions

- Use with amantadine may increase side effects
- Benztropine and all other anticholinergic agents may increase serum levels and effects of digoxin
- Can lower concentration of haloperidol and other phenothiazines, causing worsening of schizophrenia symptoms
- Can decrease gastric motility, resulting in increased gastric deactivation of levodopa and reduction in efficacy



**Other Warnings/
Precautions**

- Use with caution in hot weather, as benztropine may increase susceptibility to heat stroke
- Anticholinergic agents have additive effects when used with drugs of abuse such as cannabinoids, barbiturates, opioids, and alcohol

Do Not Use

- In patients with glaucoma, particularly angle-closure glaucoma
- In patients with pyloric or duodenal obstruction, stenosing peptic ulcers, prostate hypertrophy or bladder neck obstructions, achalasia, or megacolon
- If there is a proven allergy to benztropine

SPECIAL POPULATIONS

Renal Impairment

- No known effects, but use with caution

Hepatic Impairment

- No known effects, but use with caution

Cardiac Impairment

- Use with caution in patients with known arrhythmias, especially tachycardia

Elderly

- Use with caution
- Elderly patients may be more susceptible to side effects



Children and Adolescents

- Do not use in children ages 3 and younger
- Generalized dystonias may respond to anticholinergic treatment, and young patients usually tolerate the medication better than the elderly
- Usual dose is 0.05 mg/kg once or twice daily



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

Breast Feeding

- Unknown if benztropine is secreted in human breast milk, but all psychotropics assumed to be secreted in breast milk
- * Recommended either to discontinue drug or bottle feed unless the potential benefit to the mother justifies the potential risk to the child
- Infants of women who choose to breast feed while on benztropine should be monitored for possible adverse effects

THE ART OF PSYCHOPHARMACOLOGY

Potential Advantages

- Extrapyramidal disorders related to antipsychotic use, particularly in acute setting

Potential Disadvantages

- Patients with long-standing extrapyramidal disorders may not respond to treatment
- Generalized dystonias (less established as treatment than trihexyphenidyl)

Primary Target Symptoms

- Tremor, akinesia, rigidity, drooling



Pearls

- First-line agent for extrapyramidal disorders related to antipsychotic use
- Useful adjunct in younger Parkinson's patients with tremor, but trihexyphenidyl is more commonly used
- Useful in the treatment of post-encephalitic Parkinson's disease and for extrapyramidal reactions, other than tardive dyskinesias
- Post-encephalitic Parkinson's patients usually tolerate higher doses better than idiopathic Parkinson's patients
- Generalized dystonias are more likely to benefit from anticholinergic therapy than focal dystonias; trihexyphenidyl is used more commonly than benztropine
- Sedation limits use, especially in older patients
- 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
- Commonly used in an oral or intramuscular formulation as needed with concomitant antipsychotics to reduce or prevent EPS



Suggested Reading

Brocks DR. Anticholinergic drugs used in Parkinson's disease: an overlooked class of drugs from a pharmacokinetic perspective. *J Pharm Pharm Sci* 1999;2(2):39–46.

Colosimo C, Gori MC, Inghilleri M. Postencephalitic tremor and delayed-onset parkinsonism. *Parkinsonism Relat Disord* 1999;5(3):123–4.

Costa J, Espírito-Santo C, Borges A, et al. Botulinum toxin type A versus anticholinergics for cervical dystonia. *Cochrane Database Syst Rev* 2005;(1):CD004312.

Hai NT, Kim J, Park ES, Chi SC. Formulation and biopharmaceutical evaluation of transdermal patch containing benztropine. *Int J Pharm* 2008;357(1–2):55–60.