ANTICHOLINERGIC AGENT

Benztropine

Cogentin (brand discontinued; generic only)

Central antimuscarinic used to treat and prevent antipsychotic-induced dystonia and parkinsonism, at the cost of real cognitive burden.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
1-4 mg/day PO; max 6 mg/day	Poorly defined; ~24 h effect	Hepatic; poorly characterized	IM/IV 15 min; PO 1-2 h

No FDA boxed warning on the current US label.

INDICATIONS

- FDA-approved as an adjunct in all forms of parkinsonism, where it addresses tremor and rigidity more than bradykinesia.
- FDA-approved for drug-induced extrapyramidal disorders other than tardive dyskinesia, including antipsychotic parkinsonism and dystonia.
- FDA-approved for acute dystonic reactions, where a parenteral dose relieves oculogyric crisis or torticollis within about 15 minutes.
- Off-label short-term prophylaxis when starting a high-potency antipsychotic in a young man at high risk of acute dystonia.
- Off-label adjunct for antipsychotic-induced akathisia, although propranolol and benzodiazepines have better supporting evidence.
- It is not effective for tardive dyskinesia and frequently worsens it, so a VMAT2 inhibitor is the correct choice there.

DOSING & TITRATION

- Typical oral dosing for drug-induced parkinsonism is **1-2 mg/day**, given once daily or divided, within a range of 0.5 to 6 mg per day.
- Acute dystonic reactions are treated with **1-2 mg IM or IV**, repeated once if needed, followed by oral therapy for 1 to 2 weeks.
- Start older adults at **0.5 mg** at bedtime and increase slowly, since confusion and urinary retention appear at low doses.
- The labeled maximum is **6 mg/day**, but doses above 2 mg per day rarely add benefit and reliably add cognitive and peripheral effects.
- Attempt a taper after 3 months of stability, since many patients no longer need it once the antipsychotic dose has settled.
- Taper over 1 to 2 weeks rather than stopping abruptly, because cholinergic rebound can produce nausea, sweating, and worsened parkinsonism.

MECHANISM OF ACTION

- Antagonizes central muscarinic receptors, particularly M1, restoring the dopamine-acetylcholine balance disrupted by striatal D2 blockade.
- Because antipsychotic D2 blockade leaves cholinergic interneurons unopposed, muscarinic blockade relieves rigidity, tremor, and dystonia.
- Weak inhibition of presynaptic dopamine reuptake adds a small dopaminergic effect that contributes to its use in parkinsonism.
- Antihistaminic activity accounts for some sedation and for the overlap in effect with diphenhydramine in acute dystonia.
- Peripheral muscarinic blockade produces the dry mouth, blurred vision, constipation, urinary retention, and tachycardia seen clinically.

PHARMACOKINETICS

- Onset is within 15 minutes after intramuscular or intravenous administration and about 1 to 2 hours after an oral dose.
- Duration of action is long at roughly 24 hours, which allows convenient once or twice daily oral dosing.
- Human pharmacokinetic data are limited and the elimination half-life has never been well characterized in published studies.
- Metabolism is hepatic with a poorly defined enzymatic route, and elimination pathways have not been fully mapped.
- The long duration means anticholinergic effects can persist for a day or more after the last dose is taken.

ADVERSE EFFECTS

- Dry mouth, blurred vision, constipation, and urinary hesitancy are dose-related and affect the majority of patients at higher doses.
- Cognitive impairment with memory and attention deficits is common and often unrecognized, and it worsens antipsychotic-related cognitive burden.
- Confusion, agitation, and frank anticholinergic delirium occur most often in older adults and in patients on other antimuscarinic drugs.
- Anhidrosis with heat intolerance can cause hyperthermia during exertion or hot weather, a risk shared with antipsychotics themselves.
- Tachycardia, urinary retention, and precipitation of narrow-angle glaucoma are the peripheral effects most likely to require stopping.
- Benztropine can be misused for its euphoriant and hallucinogenic effects at high doses, particularly in institutional settings.

MONITORING

- Review continued need at every visit and attempt a taper after the antipsychotic dose has been stable for about 3 months.
- Screen for constipation, urinary hesitancy, dry eyes, and blurred vision, all of which respond to dose reduction.
- Assess cognition and orientation at each visit in older patients, since anticholinergic delirium can develop insidiously.
- Check for narrow-angle glaucoma risk before starting and ask about eye pain, halos, or visual change during therapy.
- Track total anticholinergic burden across the medication list, including antihistamines, tricyclics, and bladder antimuscarinics.

INTERACTIONS & CAUTIONS

- Additive anticholinergic toxicity with tricyclic antidepressants, first-generation antihistamines, oxybutynin, and low-potency antipsychotics.
- Directly opposes cholinesterase inhibitors such as donepezil and rivastigmine, negating cognitive benefit in dementia.
- Slowed gastric emptying can alter absorption of other drugs, and reduced gut motility raises the risk of ileus with opioids.
- Combining with drugs that impair sweating, including antipsychotics and topiramate, increases the risk of heat stroke in hot conditions.
- Contraindicated in narrow-angle glaucoma and in children under 3 years, and used with great caution in myasthenia gravis and prostatic obstruction.

SPECIAL POPULATIONS

- Pregnancy data are limited; use only when extrapyramidal symptoms clearly require treatment and prefer the lowest effective dose.
- Lactation data are sparse and anticholinergics may reduce milk supply, so monitor infant feeding and maternal milk production.
- Contraindicated under age 3 and used cautiously in older children, where dystonia can usually be managed with diphenhydramine.
- Older adults appear on Beers criteria for benztropine because of delirium, falls, and urinary retention risk; avoid where possible.
- No formal renal or hepatic dose adjustments exist, but reduce the dose when either organ system is significantly impaired.

PRESCRIBING PEARLS

- Benztropine worsens tardive dyskinesia; use a VMAT2 inhibitor instead and taper the anticholinergic.
- Reassess the need every few months; many patients stay on it for years without ongoing indication.
- For acute dystonia, **1-2 mg IM** works within 15 minutes and should be followed by a week of oral dosing.

References

American Geriatrics Society Beers Criteria Update Expert Panel. (2023). American Geriatrics Society 2023 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society, 71*(7), 2052-2081. https://doi.org/10.1111/jgs.18372

American Psychiatric Association. (2021). *The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia* (3rd ed.). https://psychiatryonline.org/guidelines

Bhidayasiri, R., Fahn, S., Weiner, W. J., Gronseth, G. S., Sullivan, K. L., & Zesiewicz, T. A. (2013). Evidence-based guideline: Treatment of tardive syndromes. *Neurology, 81*(5), 463-469. https://doi.org/10.1212/WNL.0b013e31829d86b6

Desmarais, J. E., Beauclair, L., & Margolese, H. C. (2012). Anticholinergics in the era of atypical antipsychotics: Short-term or long-term treatment? *Journal of Psychopharmacology, 26*(9), 1167-1174. https://doi.org/10.1177/0269881112447988

MedlinePlus. (2023). *Benztropine*. U.S. National Library of Medicine. https://medlineplus.gov/druginfo/meds/a682155.html

Rathbone, J., & Soares-Weiser, K. (2006). Anticholinergics for neuroleptic-induced acute akathisia. *Cochrane Database of Systematic Reviews*, (4), CD003727. https://doi.org/10.1002/14651858.CD003727.pub3

Stahl, S. M. (2021). *Stahl's essential psychopharmacology: Neuroscientific basis and practical applications* (5th ed.). Cambridge University Press.

NOTE

References follow APA 7th edition style. Dosing, boxed warnings, and interaction data change; confirm every clinical decision against the current FDA prescribing information (DailyMed) and your institution's formulary. This sheet is an educational quick reference and does not replace the full label or clinical judgment.