



## Benzotropine

Updated: July 20, 2017.

## OVERVIEW

### Introduction

Benzotropine is an anticholinergic agent used predominantly in the symptomatic therapy of Parkinson disease and movement disorders. Benzotropine has not been associated with serum enzyme elevations during treatment and has not been linked to cases of clinically apparent acute liver injury.

### Background

Benzotropine (benz' troe peen) is an anticholinergic agent that blocks the central cholinergic receptors helping to balance cholinergic transmission in the basal ganglia. Benzotropine may also block dopamine reuptake and storage in central sites thus increasing dopaminergic activity. The exact mechanism(s) by which the anticholinergic agents are beneficial for symptoms of Parkinson disease is unknown. They are used largely in early Parkinsonism and as adjunctive therapy with levodopa or more potent antiparkinson disease agents. Benzotropine was approved for use in the United States in 1954 and has been in common use since. Current indications include therapy of symptomatic Parkinson disease as well as drug induced extrapyramidal syndromes. Benzotropine in parenteral forms is also used for therapy of acute dystonic reactions. Benzotropine is available in tablets of 0.5, 1 and 2 mg, and in liquid solution for injection (2 mL ampoules; 1 mg/mL) in generic forms and under the brand name of Cogentin. The recommended dose is 0.5 to 6 mg daily. Common side effects are due to its anticholinergic activity and include nervousness, drowsiness, confusion, tachycardia, blurred vision, constipation, dry mouth, nausea and urinary retention.

### Hepatotoxicity

Benzotropine has not been reported to cause serum aminotransferase elevations, but it has not been evaluated for effects on serum enzyme levels in a prospective manner. Despite its use for more than 50 years, there have been no reports of benzotropine liver injury in the literature and it must be a very rare cause of liver injury, if it occurs at all. Absence of liver injury is typical of anticholinergic agents and may relate to the low doses used (less than 10 mg daily).

Likelihood score: E (unlikely cause of clinically apparent liver injury).

Drug Class: [Antiparkinson Agents](#), [Anticholinergic Agents](#)

Other Drugs in the Subclass, Anticholinergic Agents: [Biperiden](#), [Trihexyphenidyl](#)

## PRODUCT INFORMATION

### REPRESENTATIVE TRADE NAMES

Benztropine – Generic, Cogentin®

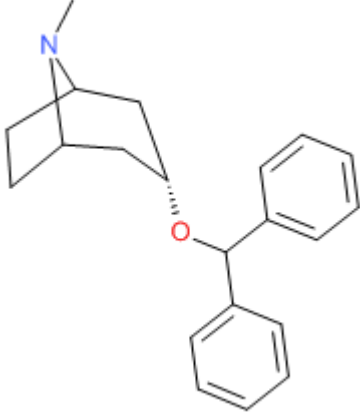
### DRUG CLASS

Antiparkinson Agents

### COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

## CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Benzotropine	86-13-5	C <sub>21</sub> H <sub>25</sub> N-O	 <p>The chemical structure of Benzotropine is shown. It consists of a bicyclic tropane ring system (8-azabicyclo[3.2.1]octane) with a methyl group on the nitrogen atom. The tropane ring is connected via an oxygen atom to a chiral center. This chiral center is also bonded to two phenyl rings. The oxygen atom is shown with a dashed bond to the tropane ring, indicating its stereochemistry.</p>

## REFERENCES

References updated: 20 July 2017

Zimmerman HJ. Antiparkinsonism drugs. In, Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999, pp. 715-7.

*(Expert review of hepatotoxicity published in 1999; among anticholinergic agents, "only trihexyphenidyl has been incriminated in hepatic injury"; other antiparkinsonism drugs discussed include levodopa, lergotrile [no longer available], pergolide and bromocriptine).*

Larrey D, Ripault MP. Hepatotoxicity of psychotropic drugs and drugs of abuse. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier Inc, 2013, pp. 443-62.

*(Review of hepatotoxicity of agents acting on the central nervous system).*

Standaert DG, Roberson ED. Treatment of central nervous system degenerative disorders. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 609-28.

*(Textbook of pharmacology and therapeutics).*

McDowell F. Symposium on levodopa in Parkinson's disease. Clinical and pharmacological aspects. Clinical laboratory abnormalities. Clin Pharmacol Ther 1971; 12: 335-9. PubMed PMID: 4102803.

*(Retrospective analysis of laboratory abnormalities arising in 974 patients with Parkinson disease treated with levodopa; AST elevations occurred in 9% of 5427 determinations, but were usually mild and transient returning to normal in 1-2 months without dose adjustment; AST levels rose to 1600 U/L in one patient who later died of complications of diabetes).*

Lambert D, Waters CH. Comparative tolerability of the newer generation antiparkinsonian agents. Drugs Aging 2000; 16: 55-65. PubMed PMID: 10733264.

*(Review of mechanism of action, tolerability and safety of selegiline, pramipexole, ropinirole, tolcapone and entacapone in Parkinson disease).*

Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. Hepatology 2010; 52: 2065-76. PubMed PMID: 20949552.

*(Among 1198 patients with acute liver failure enrolled in a US prospective study between 1998 and 2007, 133 were attributed to drug induced liver injury, but none were attributed to agents used for Parkinson disease).*

Björnsson ES, Bergmann OM, Björnsson HK, Kvaran RB, Olafsson S. Incidence, presentation, and outcomes in patients with drug-induced liver injury in the general population of Iceland. Gastroenterology 2013; 144: 1419-25,1425. PubMed PMID: 23419359.

*(In a population based study of drug induced liver injury from Iceland, 96 cases were identified over a 2 year period, but none of the 96 were attributed to an agent used to treat Parkinson disease).*

Drugs for Parkinson's disease. Treat Guidel Med Lett 2013; 11 (135): 101-6. PubMed PMID: 24165688.

*(Concise review of recommendations for therapy of Parkinson disease with description of mechanisms of action, efficacy and adverse events).*

Hernández N, Bessone F, Sánchez A, di Pace M, Brahm J, Zapata R, A Chirino R, et al. Profile of idiosyncratic drug induced liver injury in Latin America: an analysis of published reports. Ann Hepatol 2014; 13: 231-9. PubMed PMID: 24552865.

*(Among 176 reports of drug induced liver injury from Latin America published between 1996 and 2012, none were attributed to an agent to treat Parkinson disease).*

Chalasan N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, et al.; United States Drug Induced Liver Injury Network. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN Prospective Study. Gastroenterology 2015; 148: 1340-52. PubMed PMID: 25754159.

*(Among 899 cases of drug induced liver injury from the US enrolled in a prospective database between 2004 and 2012, none were attributed to an agent used to treat Parkinson disease).*