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NLM Citation: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Trospium. [Updated 2023 Jul 12].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Trospium

Updated: July 12, 2023.

OVERVIEW

Introduction

Trospium is an antispasmotic and anticholinergic agent used to treat urinary incontinence and overactive bladder syndrome. Trospium has not been implicated in causing liver enzyme elevations or clinically apparent acute liver injury.

Background

Trospium (trose' pee um) is a synthetic anticholinergic agent that inhibits muscarinic actions of acetylcholine on autonomic nerve endings, decreasing secretions and inhibiting gastrointestinal and bladder motility. Trospium increases bladder capacity and decreases bladder contractions and the urgency of urination. Trospium was approved for use in the United States in 1975 and current indications are limited to overactive bladder syndrome with symptoms of urinary urgency, frequency or incontinence. Trospium is available in standard tablets of 20 mg and in extended release [ER] capsules of 60 mg in several generic forms and previously under the brand name Sanctura. The recommended adult oral dose is 20 mg once or twice daily for the standard and 60 mg once daily for the ER formulation. Common side effects are those of parasympathetic stimulation and include dryness of the mouth and eyes, decreased sweating, headache, visual blurring, constipation, urinary retention, restlessness, confusion, and hallucinations. Rare but potentially severe adverse reactions include acute narrow angle glaucoma, acute urinary retention, gastric retention and stasis, neurologic symptoms and worsening of neurologic diseases, prolongation of the QTc interval, and severe hypersensitivity reactions.

Hepatotoxicity

In several large prospective clinical trials in patients with overactive bladder syndrome, trospium was not associated with an increased rate of serum aminotransferase elevations as compared to placebo therapy. Furthermore, despite almost 50 years of clinical use, there have been no case reports of jaundice or clinically apparent liver injury attributed to trospium therapy. Thus, liver injury with symptoms or jaundice due to trospium must be very rare if it occurs at all.

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

Mechanism of Injury

Trospium has not been linked to cases of liver injury. Trospium is probably metabolized in the liver, but its metabolic pathways have not been defined; it is not metabolized and is not affected by the microsomal P450 enzyme system.

Drug Class: Anticholinergic Agents

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Trospium – Generic, Sanctura® *(Trade name discontinued)*

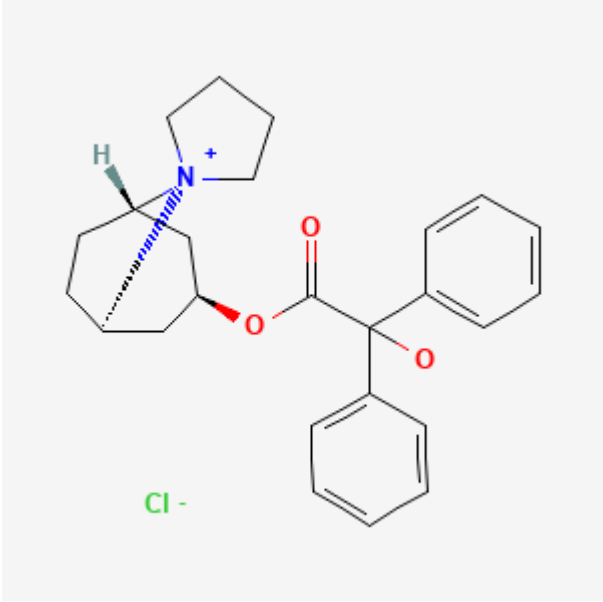
DRUG CLASS

Anticholinergic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Trospium	10405-02-4	C25-H30-Cl-N-O3	

ANNOTATED BIBLIOGRAPHY

References updated: 12 July 2023

Abbreviations: ER, extended release.

Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999.

(Expert review of hepatotoxicity published in 1999 before the availability of trospium and other therapies of overactive bladder syndrome).

Brown JH, Brandl K, Wess J. Therapeutic uses of muscarinic receptor antagonists: Muscarinic receptor agonists and antagonists. In, Brunton LL, Hilal-Dandan R, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 13th ed. New York: McGraw-Hill, 2018, pp. 156-9.

(Textbook of pharmacology and therapeutics).

Cardozo L, Chapple CR, Toozs-Hobson P, Grosse-Freese M, Bulitta M, Lehmacher W, Strösser W, et al. Efficacy of trospium chloride in patients with detrusor instability: a placebo-controlled, randomized, double-blind, multicentre clinical trial. BJU Int. 2000;85:659-64. PubMed PMID: 10759661.

(Among 208 adults with "detrusor instability" treated with trospium [20 mg] or placebo twice daily for 3 weeks, bladder capacity increased with trospium but not with placebo, while adverse event rates were similar in the two groups [68% vs 62%]; no mention of ALT elevations or hepatotoxicity).

Singh-Franco D, Machado C, Tuteja S, Zapantis A. Trospium chloride for the treatment of overactive bladder with urge incontinence. Clin Ther 2005; 27: 511-30. PubMed PMID: 15978301.

(Systematic review of efficacy and safety of trospium found major side effects to be dry mouth, constipation, and gastrointestinal upset; rare, post-marketing adverse events included Stevens Johnson syndrome, but no mention of hepatotoxicity or ALT elevations).

Rudy D, Cline K, Harris R, Goldberg K, Dmochowski R. Multicenter phase III trial studying trospium chloride in patients with overactive bladder. Urology. 2006;67:275-80. PubMed PMID: 16461077.

(Among 658 adults with symptomatic overactive bladder syndrome treated with trospium [20 mg] or placebo twice daily for 12 weeks, numbers of micturition, urgency and incontinence episodes were slightly less with trospium beginning at week 1, while adverse event rates were higher for dry mouth and constipation; no mention of ALT elevations but "no clinically meaningful differences were found between the treatment groups in clinical laboratory data").

Staskin D, Sand P, Zinner N, Dmochowski R; Trospium Study Group. Once daily trospium chloride is effective and well tolerated for the treatment of overactive bladder: results from a multicenter phase III trial. J Urol 2007;178(3 Pt 1):978-83. PubMed PMID: 17632131.

(Among 601 adults with symptomatic overactive bladder syndrome treated with an extended release [ER] form of trospium [60 mg] or placebo once daily for 12 weeks, symptoms improved modestly with trospium compared to placebo, while adverse events included dry mouth [9% vs 3%] and constipation [9% vs 1%]; there were no treatment related serious adverse events; no mention of ALT elevations or hepatotoxicity).

Novara G, Galfano A, Secco S, D'Elia C, Cavalleri S, Ficarra V, Artibani W. A systematic review and meta-analysis of randomized controlled trials with antimuscarinic drugs for overactive bladder. Eur Urol 2008; 54: 740-63. PubMed PMID: 18632201.

(Systematic review of efficacy and safety of drugs for overactive bladder including tolterodine, propiverine, solifenacin, darifenacin, fesoterodine and oxybutynin; common side effects included dry mouth and constipation; hepatotoxicity and ALT elevations were not mentioned).

Chalasani N, Fontana RJ, Bonkovsky HL, Watkins PB, Davern T, Serrano J, Yang H, Rochon J; Drug Induced Liver Injury Network (DILIN). Causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States. Gastroenterology 2008; 135: 1924-34. PubMed PMID: 18955056.

(Among 300 cases of drug induced liver disease in the US collected between 2004 and 2008, none were attributed to anticholinergics or drugs for overactive bladder).

Biastre K, Burnakis T. Trospium chloride treatment of overactive bladder. Ann Pharmacother 2009; 43: 283-95. PubMed PMID: 19193592.

(Review of pharmacology, metabolism, efficacy, and safety of trospium; common side effects are dry mouth [22%] and constipation [9%]; no mention of hepatotoxicity or ALT elevations).

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 anticholinergics or drugs for overactive bladder syndrome).

Ferrajolo C, Capuano A, Verhamme KM, Schuemie M, Rossi F, Stricker BH, Sturkenboom MC. Drug-induced hepatic injury in children: a case/non-case study of suspected adverse drug reactions in VigiBase. Br J Clin Pharmacol 2010; 70: 721-8. PubMed PMID: 21039766.

(Among 624,673 adverse event reports in children between 2000 and 2006 in the WHO VigiBase, 1% were hepatic, but no anticholinergic was listed among the 41 most frequently implicated agents).

Shamliyan T, Wyman JF, Ramakrishnan R, Sainfort F, Kane RL. Benefits and harms of pharmacologic treatment for urinary incontinence in women: a systematic review. Ann Intern Med 2012; 156: 861-74. PubMed PMID: 22711079.

(Systematic review of the safety and efficacy of drugs used for urinary incontinence including fesoterodine, tolterodine, oxybutynin, solifenacin and trospium; most had modest effectiveness; hepatotoxicity was not mentioned).

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. 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 were attributed to mirabegron or drugs for overactive bladder syndrome).

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.

(Systematic review of literature of drug induced liver injury in Latin American countries published from 1996 to 2012 identified 176 cases, but none were attributed to drugs used for overactive bladder syndrome).

Maman K, Aballea S, Nazir J, Desroziers K, Neine ME, Siddiqui E, Odeyemi I, et al. Comparative efficacy and safety of medical treatments for the management of overactive bladder: a systematic literature review and mixed treatment comparison. Eur Urol. 2014;65:755-65. PubMed PMID: 24275310.

(Systematic review of literature on medical therapies for overactive bladder identified 44 controlled trials demonstrating similar efficacy among 6 anticholinergics and a single beta-3 adrenergic agonist [mirabegron] when compared to placebo, but less dry mouth with mirabegron than with anticholinergic agents; no mention of ALT elevations or hepatotoxicity).

Chalasani 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: 1340-1352.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, none were attributed to mirabegron or other agents for overactive bladder syndrome).

Thiagamoorthy G, Cardozo L, Srikrishna S. Drug therapy for an overactive bladder. Womens Health (Lond) 2015; 11: 445-8. PubMed PMID: 26238677.

(Overactive bladder is defined as urinary urgency, usually with frequency and nocturia with or without incontinence in the absence of infection or other known cause, medical therapy being use of anticholinergics or beta-3 adrenergic receptor agonists such as mirabegron or vibegron which have fewer side effects than typical anticholinergics).

Drugs for overactive bladder. Med Lett Drugs Ther. 2023;65:41-45. PubMed PMID: 36897601.

(Concise review of drugs approved for therapy of overactive bladder in the US including anticholinergic agents [darifenacin, fesoterodine, oxbutynin, solifenacin, tolterodine and trospium] and beta-3 adrenergic receptor agonists [mirabegron and vibegron], including clinical efficacy, safety, and costs; no mention of ALT elevations or hepatotoxicity of any of the agent discussed).