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Diethylpropion

Updated: January 3, 2018.

OVERVIEW

Introduction

Diethylpropion is a sympathomimetic amine and anorectic agent used for the short-term therapy of obesity. Diethylpropion has not been linked to either serum enzyme elevations or to clinically apparent acute liver injury.

Background

Diethylpropion (dye eth" il proe' pee on) is a structural analogue to amphetamine and has similar activity in suppressing appetite, but has few of the other central nervous system effects of amphetamines and less abuse potential. Diethylpropion was approved as a therapy for obesity in the United States in 1959 and is recommended only for short term use (less than 12 weeks). Diethylpropion is available by prescription as 25 mg immediate release and 75 mg controlled release tablets in generic forms and formerly under the trade name Tenuate. The usual dose is 75 mg daily either as 25 mg (immediate release) 1 hour before meals or 75 mg (controlled release) once daily. Diethylpropion is a Schedule IV controlled substance, meaning that it has a proven but low potential for abuse and has an accepted medical use. Common side effects include nervousness, excitability, insomnia, headache, dry mouth, sweating, nausea, constipation, and thirst. Rare severe adverse events include atrial fibrillation, acute psychosis and pulmonary hypertension.

Hepatotoxicity

Diethylpropion has not been linked to an increased rate of serum enzyme elevations during therapy; however, actual results of ALT monitoring during diethylpropion therapy have rarely been reported. Despite long term availability and wide use of diethylpropion, there have been no published reports linking it to clinically apparent acute liver injury.

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

Mechanism of Injury

The safety of diethylpropion is perhaps due to its rapid urinary excretion. Nevertheless, it is extensively metabolized in the liver and some of the metabolites are biologically active.

Drug Class: Weight Loss Agents

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Diethylpropion – Generic, Tenuate®

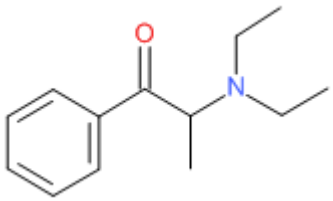
DRUG CLASS

Weight Loss Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Diethylpropion	90-84-6	C13-H19-N-O	

ANNOTATED BIBLIOGRAPHY

References updated: 03 January 2018

Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999, pp. 483-91.

(Expert review of hepatotoxicity published in 1999; diethylpropion is not discussed).

Westfall TC, Westfall DP. Adrenergic agonists and antagonists. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 277-334.

(Textbook of pharmacology and therapeutics; diethylpropion is discussed as a sympathomimetic agent used for weight loss).

Carney DE, Tweddell ED. Double blind evaluation of long acting diethylpropion hydrochloride in obese patients from a general practice. Med J Aust 1975; 1: 13-5. PubMed PMID: 1092973.

(102 obese patients enrolled in controlled trial of diethylpropion vs placebo for 16 weeks with subsequent cross-over; there were no serious adverse events and side effects were mild and transient; no mention of ALT elevations or hepatotoxicity).

Altschuler S, Conte A, Sebok M, Marlin RL, Winick C. Three controlled trials of weight loss with phenylpropanolamine. Int J Obes 1982; 6: 549-56. PubMed PMID: 6761288.

(Controlled trial of phenylpropanolamine-caffeine vs placebo vs mazindol vs diethylpropion in 201 obese patients; adverse reactions included dry mouth, diarrhea, constipation and diuresis; no serious adverse events and no mention of ALT elevations or hepatotoxicity).

Parsons WB Jr. Controlled-release diethylpropion hydrochloride used in a program for weight reduction. Clin Ther 1981; 3: 329-35. PubMed PMID: 7471128.

(49 obese patients were treated with placebo vs diethylpropion for 12 weeks; side effects included headaches, dry mouth, nervousness and nausea; no serious adverse events or liver injury occurred; ALT monitoring was not done).

Bray GA. A concise review on the therapeutics of obesity. Nutrition 2000 16: 953-60. PubMed PMID: 11054601.

(Review of drug treatment of obesity; hepatotoxicity is not discussed).

Haddock CK, Poston WS, Dill PL, Foreyt JP, Ericsson M. Pharmacotherapy for obesity: a quantitative analysis of four decades of published randomized clinical trials. Int J Obes Relat Metab Disord 2002; 26: 262-73. PubMed PMID: 11850760.

(Metaanalysis of published studies of antiobesity medications; diethylpropion was evaluated in 13 studies published between 1965-83; no discussion of side effects).

Colman E. Anorectics on trial: a half century of federal regulation of prescription appetite suppressants. Ann Intern Med 2005; 143: 380-5. PubMed PMID: 6144896.

(History of the approval of medications for obesity from initial agents approved in 1947 to sibutramine in 1997; diethylpropion was first approved in 1959, before the Kefauver-Harris amendment requiring proof of efficacy from controlled trials).

Li Z, Maglione M, Tu W, Mojica W, Arterburn D, Shugarman LR, Hilton L, et al. Meta-analysis: pharmacologic treatment of obesity. Ann Intern Med 2005; 142: 532-46. PubMed PMID: 15809465.

(Systematic review of efficacy and safety of medications for obesity; diethylpropion was evaluated in 9 placebo controlled trials of therapy for 6 to 52 weeks and was associated with modest additional weight loss; no data on adverse events were reported but evidently there were no serious adverse events attributed to therapy).

Bray GA. Drug Insight: appetite suppressants. Nat Clin Pract Gastroenterol Hepatol 2005; 2: 89-95. PubMed PMID: 16265126.

(Review of the mechanism of action and clinical efficacy of drugs that suppress appetite including sympathomimetic agents [amphenatmine, phentermine, sibutramine], serotonin reuptake inhibitors [bupropion, fenfluramine, fluoxetine], GABAergic agents [topiramate, zonisamide], cannabinoid antagonists [rimonabant] and various peptides [leptin, neuropeptide Y, melanocortin-4]).

Ioannides-Demos LL, Proietto J, Tonkin AM, McNeil JJ. Safety of drug therapies used for weight loss and treatment of obesity. Drug Saf 2006; 29: 277-302. PubMed PMID: 16569079.

(Review of safety of drug therapy of obesity; the only mention of liver adverse events was "a case of reversible hepatotoxicity associated with sibutramine").

Cercato C, Roizenblatt VA, Leança CC, Segal A, Lopes Filho AP, Mancini MC,Halpern A. A randomized double-blind placebo-controlled study of the long-term efficacy and safety of diethylpropion in the treatment of obese subjects. Int J Obes (Lond) 2009;33: 857-65. PubMed PMID: 19564877.

(Randomized controlled trial of diethylpropion vs placebo for 24 weeks and open label use thereafter; common side effects were dry mouth, insomnia, constipation, headache and dizziness; no serious adverse events or hepatotoxicity).

Kang JG, Park CY. Anti-obesity drugs: a review about their effects and safety. Diabetes Metab J 2012; 36: 13-25. PubMed PMID: 2363917.

(Review of the safety and efficacy of current and potentially future medications for obesity; mentions that no serious adverse events have been reported in controlled trials of diethylpropion).

Cheung BM, Cheung TT, Samaranayake NR. Safety of antiobesity drugs. Ther Adv Drug Saf 2013; 4: 171-81. PubMed PMID: 25114779.

(Systematic review of the literature on the efficacy and safety of drugs for weight loss; diethylpropion is described as effective in short term weight loss and generally with mild-to-moderate adverse events which are largely cardiovascular; no mention of hepatotoxicity or ALT elevations).

Suplicy H, Boguszewski CL, Dos Santos CM, do Desterro de Figueiredo M, Cunha DR, Radominski R. A comparative study of five centrally acting drugs on the pharmacological treatment of obesity. Int J Obes (Lond) 2014; 38: 1097-103. PubMed PMID: 24287940.

(Among 174 obese women treated with diethylpropion, fenproporex, mazindol, fluoxetine or sibutramine for 52 weeks, weight loss was greater with diethylpropion than placebo, but dry mouth, constipation, insomnia, anxiety and irritability were more common; no serious adverse events occurred; ALT levels not mentioned).

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 of them were attributed to drugs for weight loss).

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: 1340-52.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, none were due to diethylpropion).