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Nabilone

Updated: April 10, 2014.

OVERVIEW

Introduction

Nabilone is an orally available cannabinoid agonist that is used to treat nausea and vomiting and to stimulate appetite, particularly in patients with wasting disease or cachexia. Nabilone is associated with a minimal rate of serum enzyme elevations during therapy and has not been linked to cases of clinically apparent liver injury with jaundice.

Background

Nabilone (Nab' i lone) is a synthetic cannabinoid which is similar to the principal psychoactive constituent of the marijuana plant (Cannabis sativa). Nabilone is a partial agonist of the cannabinoid receptors which are found in the central nervous system (CB1 receptor), but also peripherally (largely CB2 receptors). Activation of CB receptors results in effects on appetite, mood, cognition, memory and perception. Nabilone therapy has been shown to decrease nausea and vomiting in patients undergoing cancer chemotherapy. Nabilone was approved for use in the United States in 1985 and current indications are prevention of cancer chemotherapy associated nausea and vomiting. Nabilone is available as 1 mg capsules under the brand name Cesamet. The typical adult oral dose is 1 to 2 mg twice daily, the initial dose being 1 to 3 hours before the chemotherapeutic agent is given. Common side effects include fatigue, somnolence, dizziness, euphoria, abnormal thinking, paranoid reactions, conjunctivitis, diarrhea, nausea, vomiting and abdominal pain. Rare side effects include hallucinations and seizures. Nabilone is classified as a Schedule II drug, indicating that it has clear potential for physical and psychological dependency and abuse.

Hepatotoxicity

Serum aminotransferase elevations during nabilone therapy are not common, generally mild and similar in to the rate in controls who are receiving cancer chemotherapy. There have been no convincing cases of clinically apparent liver injury attributable to nabilone published in the literature and, thus, significant liver injury from nabilone must be exceeding rare, if it occurs at all.

Mechanism of Injury

Nabilone is metabolized by the liver and undergoes extensive first-pass metabolism to both active and inactive metabolites. Despite its hepatic metabolism by CYP microsomal enzymes, it has not been implicated in causing drug-drug interactions. The lack of reported cases of liver injury and low rate of drug-drug interactions due to nabilone may be due to the low doses and limited duration of typical therapy.

Drug Class: Gastrointestinal Agents, Antiemetics

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Nabilone – Cesamet®

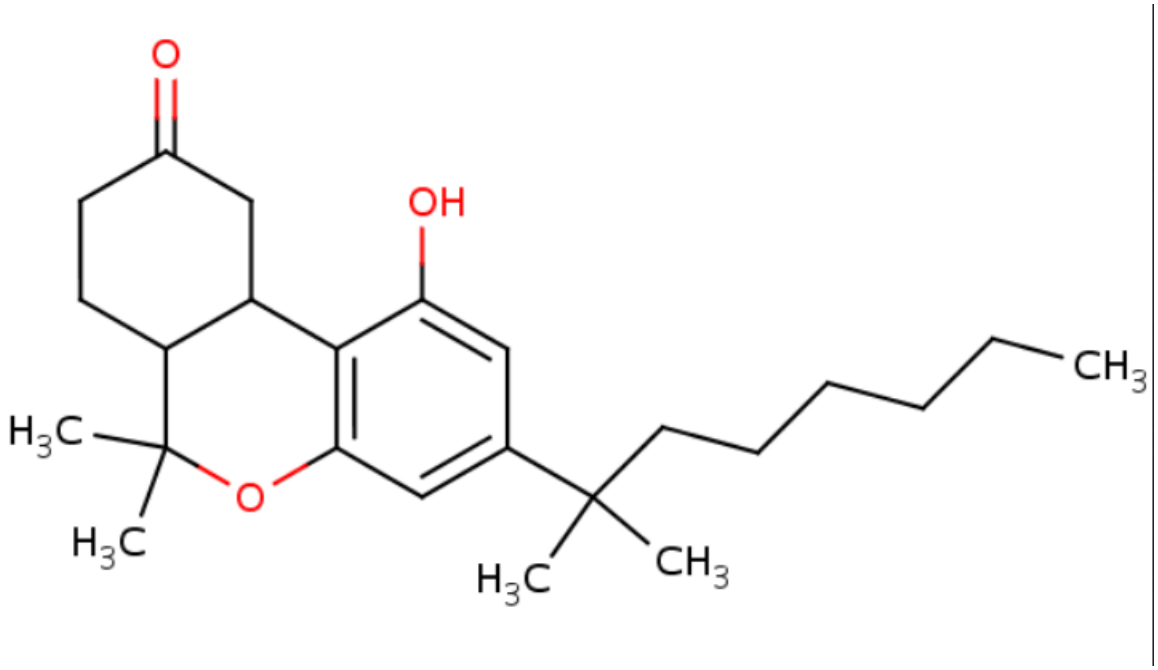
DRUG CLASS

Gastrointestinal Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Nabilone	51022-71-0	C24-H36-O3	

ANNOTATED BIBLIOGRAPHY

References updated: 10 April 2014

Zimmerman HJ. Antiemetic and prokinetic compounds. Miscellaneous drugs and diagnostic chemicals. In, Zimmerman, HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999: pp. 721.

(Expert review of hepatotoxicity published in 1999 does not discuss nabilone).

Sharkey KA, Wallace JL. Treatment of disorders of bowel motility and water flux: anti-emetics; agents used in biliary and pancreatic disease. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 1323-50.

(Textbook of pharmacology and therapeutics).

Marijuana. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 562-7.

(Compilation of short monographs on herbal medications and dietary supplements).

Fabre LF, McLendon D. The efficacy and safety of nabilone(a synthetic cannabinoid) in the treatment of anxiety. J Clin Pharmacol 1981; 21: 377S-382S. PubMed PMID: 6117575.

(Among 25 patients with anxiety disorders participating in dose finding studies of nabilone for up to 28 days, the most common side effects were dry mouth and eyes, drowsiness, headaches and insomnia; "nabilone did not alter any value in the clinical chemistry battery").

Beal JE, Olson R, Laubenstein L, Morales JO, Bellman P, Yangco B, Lefkowitz L, et al. Dronabinol as a treatment for anorexia associated with weight loss in patients with AIDS. J Pain Symptom Manage 1995; 10: 89-97 PubMed PMID: 7730690.

(Among 139 patients with AIDS-related anorexia and weight loss treated with dronabinol or placebo for up to 4 weeks, side effects included euphoria, dizziness, drowsiness and difficulty thinking and "no treatment-related toxicity was found on. laboratory tests").

Beal JE, Olson R, Lefkowitz L, Laubenstein L, Bellman P, Yangco B, Morales JO, et al. Long-term efficacy and safety of dronabinol for acquired immunodeficiency syndrome-associated anorexia. J Pain Symptom Manage 1997; 14: 7-14. PubMed PMID: 9223837.

(Among 94 patients with late stage AIDS treated with dronabinol [2.5-5 mg daily] for up to 12 months, there were "no significant changes in hematology or blood chemistry parameters").

Wissel J, Haydn T, Mueller J, Brenneis C, Berger T, Poewe W, Schelosky LD. Low dose treatment with the synthetic cannabinoid Nabilone significantly reduces spasticity-related pain: a double-blind placebo-controlled cross-over trial. J Neurol 2006; 253: 1337-41. PubMed PMID: 16988792.

(Among 13 patients with upper motor neuron disease and spasticity treated with nabilone [1 mg daily] for up to 9 weeks, pain and spasticity decreased and "no severe side effects were reported").

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, no cases were attributed to cannabinoid agonists or antiemetics).

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 antiemetic agents).

Borgelt LM, Franson KL, Nussbaum AM, Wang GS. The pharmacologic and clinical effects of medical cannabis. Pharmacotherapy 2013; 33: 195-209. PubMed PMID: 23386598.

(Review of history and status of cannabis used for medical purposes including severe pain, muscle spasms, anorexia, nausea and vomiting, and glaucoma; adverse events are common, but usually mild and reversible, most frequently dry mouth, dizziness, drowsiness, and changes in cognition and mood).

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 antiemetics).

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, the most common implicated agents being nimesulide [n=53: 30%], cyproterone [n=18], nitrofurantoin [n=17], antituberculosis drugs [n=13], and flutamide [n=12: 7%]; no cannabinoid agonist or antiemetic was listed).