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Droogsma E, Veeger N, van Walderveen P, Niemarkt S, van Asselt D. Effect of treatment gaps in elderly patients with dementia treated with cholinesterase inhibitors. Neurology. 2013;80(17):1622. Edwards K, Royall D, Hershey L, Lichter D, Ake A. Efficacy and safety of galantamine in patients with dementia with Lewy body: A 24-week open-label study. Dement Geriatr Cogn Disord. 2007;23:401. Jann MW, Small GW. Cholinesterase Inhibitors. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 9th ed. Vol. 2. Philadelphia: Lippincott Williams & Wilkins; 2009:3089. Porsteinsson AP, Grossberg GT, Mintzer J, Memantine MEM MD 12 Study Group. Memantine treatment in patients with mild to moderate Alzheimer's disease already receiving a cholinesterase inhibitor: A randomized, double-blind, placebocontrolled trial. Curr Alzheimer Res. 2008;5:83. Qassem A, Snow V, Cross JT Jr., Forcicea MA, Hopkins R Jr., Shekelle P, Adelman A, Mehr D, Schellhase K, CamposOutcalt D, Santagoida P, Owens DK. Current pharmacologic treatment of dementia: A clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. Ann Intern Med. 2008;148:370. Reisberg B, Doody R, Stoffer A, Schmidt F, Ferris S. A 24-week open label extension study on memantine in moderate to severe Alzheimer's disease. Arch Neurol. 2006;63:49. Ritchie C, Zhinchin G. Low dose, high dose, or no dose: Better prescribing of cholinesterase inhibitors for Alzheimer's disease. Int Psychogeriatr. 2013;25(4):511–515. Seltzer B. Donepezil: An update. Expert Opin Pharmacother. 2007;8:1011. Wagle KC, Rowan PJ, Poon O-YI, Kunik ME, Taffet GE, Braun UK. Initiation of cholinesterase inhibitors in an inpatient setting. Am J Alzheimer Dis Other Demen. 2013;28(4):377–383. 29.15 Disulfiram and Acamprosate Disulfiram (Antabuse) and acamprosate (Campral) are drugs used to treat alcohol dependence. Disulfiram has suffered from a reputation as a dangerous medication only suitable for highly motivated and strictly supervised drinkers because of the severe physical reactions the drug causes after drinking. Experience has shown, however, that at recommended doses it is an acceptable and safe medication for dependent drinkers seeking to sustain abstinence. The properties that constitute disulfiram's main therapeutic effect (i.e., the ability to produce unpleasant symptoms after alcohol intake, also known as disulfiram–alcohol reaction) have created that perception of dangerousness. In the most severe cases, when disulfiram is combined with alcohol serious clinical conditions can occur. These

include respiratory depression, cardiovascular collapse, acute heart failure, convulsions, loss of consciousness, and death in rare cases. These potential complications as well as the development of alternative antialcohol medications have been the limiting factors for the wider use of disulfiram. Unlike disulfiram, acamprosate, the other drug discussed in this section, does not produce aversive side effects. Acamprosate is now prescribed more commonly than disulfiram in outpatient settings, but disulfiram is prescribed more often in inpatient settings because it helps facilitate initial abstinence. Other drugs that are useful in reducing alcohol consumption include naltrexone (ReVia, Trexan), nalmefene (Revex), topiramate (Topamax), and gabapentin

(Neurontin). These agents are discussed in their respective sections. DISULFIRAM Pharmacologic Actions Disulfiram is almost completely absorbed from the gastrointestinal (GI) tract after oral administration. Its half-life is estimated to be 60 to 120 hours. Therefore, 1 or 2 weeks may be needed before disulfiram is totally eliminated from the body after the last dose has been taken. The metabolism of ethanol proceeds through oxidation via alcohol dehydrogenase to the formation of acetaldehyde, which is further metabolized to acetyl-coenzyme A (acetyl-CoA) by aldehyde dehydrogenase. Disulfiram is an aldehyde dehydrogenase inhibitor that interferes with the metabolism of alcohol by producing a marked increase in blood acetaldehyde concentration. The accumulation of acetaldehyde (to a level up to 10 times higher than occurs in the normal metabolism of alcohol) produces a wide array of unpleasant reactions, called the disulfiram–alcohol reaction, characterized by nausea, throbbing headache, vomiting, hypertension, flushing, sweating, thirst, dyspnea, tachycardia, chest pain, vertigo, and blurred vision. The reaction occurs almost immediately after the ingestion of one alcoholic drink and may last from 30 minutes to 2 hours. Blood Concentrations in Relation to Action. Plasma concentrations of disulfiram varies among individuals because of a number of factors, most notably age and hepatic function. In general, the severity of disulfiram–alcohol reaction has been shown to be proportional to the amount of the ingested disulfiram and alcohol. Nevertheless, disulfiram plasma levels are rarely obtained in clinical practice. The positive correlation between plasma concentrations of alcohol and the intensity of the reaction is described as follows: in sensitive individuals, as little as 5 to 10 mg per 100 mL increase of the plasma alcohol level may produce mild symptoms; fully developed symptoms occur at alcohol levels of 50 mg per 100 mL; and levels as high as 125 to 150 mg per 100 mL result in loss of consciousness and coma. Therapeutic Indications The primary indication for disulfiram use is as an aversive conditioning treatment for alcohol dependence. Either the fear of having a disulfiram–alcohol reaction or the memory of having had one is meant to condition the person not to use alcohol. Usually, describing the severity and the unpleasantness of the disulfiram–alcohol reaction graphically enough discourages the person from imbibing alcohol. Disulfiram treatment should be combined with such treatments as psychotherapy, group therapy, and support groups such as Alcoholics Anonymous (AA). Treatment with disulfiram requires careful monitoring because a person can simply decide not to take the medication.

Precautions and Adverse Reactions With Alcohol Consumption. The intensity of the disulfiram–alcohol reaction varies with each person. In extreme cases, it is marked by respiratory depression, cardiovascular collapse, myocardial infarction, convulsions, and death. Therefore, disulfiram is contraindicated for persons with significant pulmonary or cardiovascular disease. In addition, disulfiram should be used with caution, if at all, by persons with nephritis, brain damage, hypothyroidism, diabetes, hepatic disease, seizures, polydrug dependence, or an abnormal electroencephalogram. Most fatal reactions occur in persons who take more than 500 mg a day of

disulfiram and who consume more than 3 oz of alcohol. The treatment of a severe disulfiram–alcohol reaction is primarily supportive to prevent shock. The use of oxygen, intravenous vitamin C, ephedrine, and antihistamines has been reported to aid in recovery. Without Alcohol Consumption. The adverse effects of disulfiram in the absence of alcohol consumption include fatigue, dermatitis, impotence, optic neuritis, a variety of mental changes, and hepatic damage. A metabolite of disulfiram inhibits dopamine-βhydroxylase, the enzyme that metabolizes dopamine into norepinephrine and epinephrine, and thus may exacerbate psychosis in persons with psychotic disorders. Catatonic reactions may also occur. Drug Interactions Disulfiram increases the blood concentration of diazepam (Valium), paraldehyde, phenytoin (Dilantin), caffeine, tetrahydrocannabinol (the active ingredient in marijuana), barbiturates, anticoagulants, isoniazid (Nydrazid), and tricyclic drugs. Disulfiram should not be administered concomitantly with paraldehyde because paraldehyde is metabolized to acetaldehyde in the liver. Laboratory Interferences In rare instances, disulfiram has been reported to interfere with the incorporation of iodine-131 into protein-bound iodine. Disulfiram may reduce urinary concentrations of homovanillic acid, the major metabolite of dopamine, because of its inhibition of dopamine hydroxylase. Dosage and Clinical Guidelines Disulfiram is supplied in 250- and 500-mg tablets. The usual initial dosage is 500 mg a day taken by mouth for the first 1 or 2 weeks followed by a maintenance dosage of 250 mg a day. The dosage should not exceed 500 mg a day. The maintenance dosage range is 125 to 500 mg a day. Persons taking disulfiram must be instructed that the ingestion of even the smallest amount of alcohol will bring on a disulfiram–alcohol reaction, with all of its unpleasant

effects. In addition, persons should be warned against ingesting any alcohol-containing preparations, such as cough drops, tonics of any kind, and alcohol-containing foods and sauces. Some reactions have occurred in patients who used alcohol-based lotions, toilet water, colognes, or perfumes and inhaled the fumes; therefore, precautions must be explicit and should include any topically applied preparations containing alcohol, such as perfume. Disulfiram should not be administered until the person has abstained from alcohol for at least 12 hours. Persons should be warned that the disulfiram–alcohol reaction may occur as long as 1 or 2 weeks after the last dose of disulfiram. Persons taking disulfiram should carry identification cards describing the disulfiram–alcohol reaction and listing the name and telephone number of the physician to be called. ACAMPROSATE Pharmacologic Actions Acamprosate’s mechanism of action is not fully understood, but it is thought to antagonize neuronal overactivity related to the actions of the excitatory neurotransmitter glutamate. In part, this may result from antagonism of N-methyl-daspartate (NMDA) receptors. Indications Acamprosate is used for treating alcohol-dependent individuals seeking to continue to remain alcohol free after they have stopped drinking. Its efficacy in promoting abstinence has not been demonstrated in persons who have not undergone detoxification and who have not achieved alcohol abstinence before beginning treatment. Precautions and Adverse Effects Side effects are mostly seen early in treatment and are usually mild and transient in nature. The most common side effects are headache, diarrhea, flatulence, abdominal pain, paresthesias, and various skin reactions. No adverse events occur after abrupt withdrawal of acamprosate, even after long-term use. There is no evidence of addiction to the drug. Patients with severe renal impairment (creatinine clearance of less than 30 mL per minute) should not be given acamprosate. Drug Interactions The concomitant intake of alcohol and acamprosate does not affect the pharmacokinetics of either alcohol or acamprosate. Administration of disulfiram or diazepam does not affect the pharmacokinetics of acamprosate. Coadministration of naltrexone with acamprosate produces an increase in concentrations of acamprosate. No

adjustment of dosage is recommended in such patients. The pharmacokinetics of

naltrexone and its major metabolite 6-β-naltrexol were unaffected after coadministration with acamprosate. During clinical trials, patients taking acamprosate concomitantly with antidepressants more commonly reported both weight gain and weight loss compared with patients taking either medication alone. Laboratory Interferences Acamprosate has not been shown to interfere with commonly done laboratory tests. Dosage and Clinical Guidelines It is important to remember that acamprosate should not be used to treat alcohol withdrawal symptoms. It should only be started after the individual has been successfully weaned off alcohol. Patients should show a commitment to remaining abstinent, and treatment should be part of a comprehensive management program that includes counseling or support group attendance. Each tablet contains acamprosate calcium 333 mg, which is equivalent to 300 mg of acamprosate. The dose of acamprosate is different for different patients. The recommended dosage is two 333-mg tablets (each dose should total 666 mg) taken three times daily. Although dosing may be done without regard to meals, dosing with meals was used during clinical trials and is suggested as an aid to compliance in patients who regularly eat three meals daily. A lower dose may be effective in some patients. A missed dose should be taken as soon as possible. However, if it is almost time for the next dose, the missed dose should be skipped, and then the regular dosing schedule should be resumed. Doses should not be doubled up. For patients with moderate renal impairment (creatinine clearance of 30 to 50 mL minute), a starting dosage of one 333mg tablet taken three times daily is recommended. People with severe renal insufficiency should not take acamprosate. REFERENCES Ducharme LJ, Knudsen HK, Roman PM. Trends in the adoption of medications for alcohol dependence. J Clin Psychopharmacol. 2006;26(Suppl 1):S13. Fuehrlein BS, Gold MS. Medication-assisted recovery in alcohol and opioid dependence. Dir Psychiatry. 2013;33(1):15–27. Ivanov I. Disulfiram and acamprosate. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan & Sadock’s Comprehensive Textbook of Psychiatry. 9th ed. Vol. 2. Philadelphia: Lippincott Williams & Wilkins; 2009:3099. Johnson BA. Update on neuropharmacological treatments for alcoholism: Scientific basis and clinical findings. Biochem Pharmacol. 2008;75(1):34. Laaksonen E, Koski-Jännes A, Salaspuro M, Ahtínen H, Alho H. A randomized, multicentre, open-label, comparative trial of disulfiram, naltrexone and acamprosate in the treatment of alcohol dependence. Alcohol. 2008;43(1):53. Mann K, Kiefer F, Spanagel R, Littleton J. Acamprosate: Recent findings and future research directions. Alcohol Clin Exp Res. 2008;32(7):1105. Niederhofer H, Staffen W. Naltrexone and disulfiram in patients with alcohol dependence and comorbid psychiatric disorders. Biol Psychiatry. 2005;57(10):1128.

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