



Disulfiram

Generic name	Disulfiram
Available brand	Antabuse
Available strengths and formulations	250-mg and 500-mg tablets
Available in generic	Yes

GENERAL INFORMATION

Disulfiram (Antabuse) was the first, and the oldest, medication approved by the U.S. Food and Drug Administration (FDA) in 1951 for treatment of alcohol dependence. Currently, there are two other medications approved by the FDA for alcohol dependence: acamprosate and naltrexone. Disulfiram is a deterrent medication that induces an adverse reaction when the person drinks. The severity of the disulfiram reaction depends on the amount of alcohol ingested. Disulfiram therapy should be used to treat those who are highly motivated to stay abstinent. By no means does disulfiram provide a cure for alcoholism. In order to have any impact on the drinking pattern of the person with chronic alcoholism, disulfiram should be used in conjunction with supportive programs that include group support therapy and counseling. Disulfiram does not reduce the craving for alcohol—it merely produces a deterrent to drinking.

Disulfiram blocks an enzyme (**acetaldehyde dehydrogenase**) in the liver that breaks down the alcohol, causing the metabolite **acetaldehyde** to accumulate. Acetaldehyde accumulation produces the symptoms of a disulfiram reaction, not unlike the effects of a bad hangover. When the person takes disulfiram, consumption of any alcohol, intentionally or unintentionally, can trigger these symptoms, also known as a **disulfiram reaction**. The potential of this adverse reaction discourages the person from drinking and reinforces abstinence.

Before prescribing disulfiram, the practitioner must obtain a complete medical history from the patient. If the patient has any history of liver disease, cardiovascular disease, stroke, diabetes mellitus, or seizures, he or she should not receive disulfiram. The practitioner must provide the patient with a clear understanding of a disulfiram reaction; family members or caregivers should receive this information as well. It is highly recommended that the patient sign an informed consent, documenting that the patient understands the consequences of ingesting alcohol and assumes the responsibility of avoiding all alcohol intake. Disulfiram should never be administered when the person is in a state of intoxication or without his or her full knowledge.

In retrospective studies, it was found that disulfiram alone is seldom successful in the treatment of alcohol dependence. Other factors are associated with achieving successful abstinence: the type, intensity, and duration of treatment programs; the management of other problems (e.g., depression); the use of community-based support groups (e.g., Alcoholics Anonymous and Narcotics Anonymous); and the

use of compliance-enhancing methods to ensure medication adherence. Abstinence rates were higher when these components of treatment were incorporated with disulfiram than when medication alone was the treatment. And, of course, it takes a motivated individual to achieve lasting abstinence.

DOSING INFORMATION

Disulfiram should not be administered until the patient has abstained from alcohol for at least 12 hours. The recommended initial dosage is 500 mg once a day for 1–2 weeks, and the dosage may be reduced to 250 mg once daily. The maintenance dosage ranges from 125 mg to 500 mg daily, but the dosage should not exceed 500 mg/day. The duration of treatment depends on the patient's adherence to the treatment program or when the patient feels self-control has been established without need of the medication.

COMMON SIDE EFFECTS

Disulfiram may cause some transient side effects (not from the disulfiram-alcohol reaction) during the first few weeks of therapy. Patients may experience mild drowsiness, sedation, tiredness, headache, nausea, metallic aftertaste, or acne eruptions. Usually, these side effects are mild and subside with continued therapy or dosage reduction.

ADVERSE REACTIONS AND PRECAUTIONS

The ingestion of alcohol, even in small amounts, in the presence of disulfiram can trigger a disulfiram-alcohol reaction not unlike a very bad hangover. Symptoms include nausea, vomiting, rapid heartbeat, throbbing headache, flushing, sweating, dizziness, shortness of breath, and low blood pressure (**hypotension**). The intensity and duration of the reaction depend on the amount of disulfiram in the system and amount of alcohol ingested and vary with each individual. The reaction can last 30–60 minutes or for several hours in more severe reactions. In rare and very severe reactions, disulfiram may induce a heart attack, arrhythmias, loss of consciousness, convulsions, and death.

Patients should be cautioned to read the labels of foods and medications for the presence of alcohol. For example, many liquid cold and cough preparations (e.g., NyQuil Cold & Flu) contain an alcohol base, and in the usual dosage it is enough to trigger a disulfiram reaction. Disulfiram is absorbed and eliminated slowly from the body. A disulfiram reaction can still occur a week after stopping the medication and then drinking alcohol.

There have been reported cases of liver toxicity associated with disulfiram. In some cases, the liver failures were fatal. Liver toxicity occurred in some patients with normal liver function, so laboratory tests may not always be helpful for routine monitoring of disulfiram-induced liver toxicity. Liver function tests should be part of routine screening before starting disulfiram to preclude patients whose liver tests are abnormal. Patients, however, are advised to stop disulfiram and notify their practitioners immediately when they detect signs and symptoms of liver problems, such as fatigue, flu-like symptoms, loss of appetite, nausea, vomiting, yellowing of the eyes or skin (**jaundice**), or dark urine.

Depression is frequently associated with alcohol dependence, and suicidality is higher in individuals with untreated depression. During the early phase of therapy, patients should be monitored closely for clinical signs of depression, especially suicidal thinking and behavior.

RISK DURING PREGNANCY AND BREAST-FEEDING

Studies have not been conducted in pregnant women to determine the safety of disulfiram in pregnancy. Disulfiram-alcohol reactions may pose grave risk to the fetus and mother in the event of alcohol inges-

tion, accidental or otherwise. The risk far outweighs any benefits of disulfiram therapy during pregnancy. Women of childbearing age should be cautioned of the potential hazards to the fetus if they become pregnant while taking this drug.

Nursing mothers should not take disulfiram because small amounts may pass into breast milk and be ingested by the baby. If stopping the drug is not an alternative, breast-feeding should not be started or should be discontinued.

POTENTIAL DRUG INTERACTIONS

Besides alcohol, disulfiram may have other clinically important drug interactions. Metronidazole (Flagyl), an antibiotic, should not be taken with disulfiram. The combination has been reported to cause acute psychosis and mental confusion in some patients. The cause is unknown. Disulfiram should be discontinued for 2 weeks prior to starting metronidazole.

The activity of warfarin (Coumadin), a blood-thinning agent, may be increased (as indicated by the international normalized ratio test [INR]) by disulfiram if taken together. The increased activity of warfarin may increase the risk of bleeding if the dosage is not adjusted.

Disulfiram may interfere with the metabolism of phenytoin (Dilantin) and fosphenytoin (Cerebyx), both anticonvulsants, and increase their blood levels, increasing the risk of toxicity. When used in combination with disulfiram, phenytoin blood levels should be checked more frequently to determine if dosage adjustments may be needed.

OVERDOSE

An acute overdose of disulfiram may be potentially fatal. The severity of toxicity depends on the amount ingested, the age and weight of the person, and if the person also ingested other medications. The effect of disulfiram overdose in children is unknown. The signs and symptoms of disulfiram overdose when taken alone include nausea, vomiting, dizziness, drowsiness, loss of coordination, seizures, and coma.

Any suspected overdose should be treated as an emergency. The person should be taken to the emergency department for observation and treatment. The prescription bottle of medication (and any other medication suspected in the overdose) should be brought along as well because the information on the prescription label can be helpful to the treating practitioner in determining the number of pills ingested.

The American Association of Poison Control Centers (www.aapcc.org) can also be contacted via their helpline at 1-800-222-1222, and they can provide the location of the local poison center.

TREATMENT SUMMARY

- **Warning:** Always let your practitioner or a family member know if you have suicidal thoughts. Notify your practitioner whenever your depressive symptoms worsen or whenever you feel unable to control suicidal urges or thoughts.
- Disulfiram is usually taken once a day or as directed by your practitioner. If you miss a dose, take it as soon as possible. If it is close to the next scheduled dose, skip the missed dose and continue on your regular dosing schedule. Do not take double doses.
- Always check for alcohol content in foods and medications. Even alcohol in topical products (e.g., aftershave lotion) sometimes can be absorbed through the skin and induce a mild disulfiram reaction.
- It is unlikely patients can succeed in maintaining abstinence with disulfiram alone and without other psychosocial intervention like support group therapy and counseling.
- If relapse occurs, do not get discouraged; discuss your drinking with your practitioner, counselor, or therapist. Continue taking disulfiram as directed, and consult your practitioner as soon as possible.

- Store the medication in its originally labeled, light-resistant container, away from heat and moisture. Heat and moisture may precipitate breakdown of your medication, and the medication may lose its therapeutic effects.
- Keep your medication out of the reach of children.
- The following Web sites can provide you and your family members with additional information:
 - Alcoholics Anonymous: www.aa.org
 - National Institute on Alcohol Abuse and Alcoholism: www.niaaa.nih.gov
 - National Organization on Fetal Alcohol Syndrome: www.nofas.org
 - National Council on Alcoholism and Drug Dependence (NCADD): <https://ncadd.org>
List of NCADD Affiliates: <https://ncadd.org/about-ncadd/our-affiliates>
 - Substance Abuse and Mental Health Services Administration (SAMHSA): www.samhsa.gov

If you have any questions about your medication, consult your medical practitioner or pharmacist.

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