

Disulfiram (Antabuse®)

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Disulfiram (Antabuse) is perhaps the most widely used treatment for alcoholism in Finland. Normally, ethanol is converted into acetaldehyde and then acetic acid before being excreted from the body. Disulfiram prevents the oxidation process, causing acetaldehyde build-up. Even in small quantities, acetaldehyde is known to cause nausea, vomiting (including damage to the oesophagus), a burning sensation on the skin, flushing and shortness of breath, also known as a disulfiram or Antabuse reaction. Other symptoms include sweating and hypotension. Severe cases may result in shock. The reaction is often extremely pronounced, making alcohol consumption almost impossible. Disulfiram is therefore acts as a deterrent against further drinking, as it does not alleviate the craving for alcohol itself. Disulfiram also has other effects, including inhibiting noradrenalin production.

Dosage

Disulfiram treatment can be commenced when the patient is no longer under the influence of alcohol. No alcohol should have been consumed in the 12-hour period preceding treatment. The patient should also be made aware of the so-called disulfiram reaction. The initial dose is 800mg daily for a few days. The dose for maintenance treatment is 100–200mg daily or 400–800mg twice weekly. The doctor can also give additional guidance for alternative doses: disulfiram can, for example, be taken “as required” in the event of high-risk situations such as parties and holidays.

Disulfiram treatment tends to be more successful if it is administered under the supervision of a healthcare professional or spouse, for example. This is particularly the case in the early stages of the treatment. The patient can sign a so-called pledge, in which they commit to the treatment for a period of six months. Without supervision, the patient may take the disulfiram sporadically, leading to a less successful outcome. Disulfiram is available by prescription from pharmacies as an effervescent tablet (Antabuse, 200mg). The tablet should be dissolved in a glass of water just before consumption. The drink has a neutral flavour. To ensure the best outcome, the disulfiram should be taken first thing in the morning.

Disulfiram is also available as an implant. The therapeutic outcomes have been poor as the disulfiram levels in the body have remained insufficient. Nowadays, the use of implants is rare.

Characteristics of disulfiram

In the body, disulfiram converts via a number of stages into the actual effective ingredient, diethyldithiocarbamic-acid-methyl ester (DDTC-Me). The effects are felt within a couple of hours. The best effect is achieved after approximately three days of treatment and wears off after 1–2 weeks. The duration of action depends on the exact dosage and personal susceptibility. Due to its long half-life, disulfiram supports abstinence, even if a patient deliberately omits a few doses. Disulfiram should never be administered “secretly”, as **the concomitant use of disulfiram and alcohol can result in organ damage or even death.**

The onset of the disulfiram reaction is extremely rapid, usually 5 to 10 minutes. The duration of the effect can vary from 30 minutes to several hours – for as long as the alcohol remains in the body. The body does not develop a tolerance to disulfiram, meaning that treatment can be continued for years. In fact, over time, the patient is further sensitised to alcohol, with even small reactions causing the disulfiram reaction.

Side effects

Although disulfiram is associated with non-alcohol-related side effects, it is generally considered very safe. The most common side effects include fatigue, headaches, upset stomach, changes in the ability to taste and bad breath. These usually wear off with time, however. Elevated liver enzyme levels and jaundice are also possible, but these will disappear as soon as treatment is discontinued. LFTs, including AST/ALT and bilirubin should be checked before treatment and monitored regularly thereafter. In the early stages of treatment, LFTs should be checked every two weeks for two months and then between two and four times a year. Nickel allergy sufferers are known to be more susceptible to the side effects of disulfiram. Less common or rare side effects include skin reactions and tremors. As with all medicines, long-term (measured in years), high-dosage use increases the risk of serious side effects. In ordinary use, however, disulfiram is considered to be a safe and well-tolerated treatment.

Disulfiram is not recommended during pregnancy and breastfeeding due to insufficient clinical evidence of the effects of the treatment on this population. It is, however, likely to be safer for the foetus than maternal alcohol consumption. Pregnant and breastfeeding women should contact their doctor before commencing or continuing treatment.

Drug interactions

Most medicines are known to interact with disulfiram (see Table 1). Please note that the information provided below is intended for broad guidance only. It is important that patients provide their doctor with full details of all medicines and any homeopathic preparations they are taking to avoid interactions. Patients can also contact their local pharmacy for further information. The interactions are due to the effect of disulfiram on a number of enzymes (CYP2C9 and CYP2E1 inhibitor). Please note that certain prescription-only medicines have a similar effect to that of disulfiram when combined with alcohol.

Table 1. Disulfiram drug interactions (indicative only).

Medicine/active ingredient	Brand name	Interaction
Warfarin (blood thinner)	Marevan	Increased effect
Amitriptyline (tricyclic antidepressant)	Triptyl	
Phenytoin (seizure medicine)	Hydantin	
Benzoiazepines (incl. diazepam)	Stesolid	
Theophylline (asthma medicine)	Retafyllin	
Fluvastatin and rosuvastatin (statins)	Lescol, Crestor	Increased disulfiram concentration
Isoniazid (antibiotic)	Tubilysin	Serious CNS effects
Caffeine	-	Increased effect of caffeine

During disulfiram treatment, patients should carefully avoid consuming anything that might contain alcohol. Some estimates suggest that the most susceptible patients experience the antabuse reaction when their blood alcohol concentration exceeds 0.05–0.1‰. As an illustration, one serving of Finnish class III lager (usually 3.7–4.7 ABV) will cause a blood alcohol concentration of 0.2‰ in an adult weighing 70kg. In effect, this means that just one sip of lager is sufficient to generate a reaction. Patients taking disulfiram should be particularly cautious with other medicinal products likely to contain alcohol, including many cough medicines. A 0.5‰ alcohol concentration is sufficient to cause a full-blown antabuse reaction, with loss of consciousness setting at 1.25–1.5‰. Patients should also avoid all foods that might contain alcohol, including alcohol-free lagers. Even alcohol-filled chocolates or a sip of communion wine are enough to set off a reaction.

Importantly, it is also possible that products containing alcohol that are applied to the skin or mucous membrane – such as antiseptic lotions, aftershaves, deodorants and mouthwashes – may cause an antabuse reaction. It would be difficult to issue recommendations for the above products due to the number of variables involved, i.e. the strength of the antiseptic used, the area treated, simultaneous use of any other products containing alcohol, etc. There are some reports

of antabuse reactions caused by the concomitant use of these types of everyday products but they tend to be isolated incidents. As such, it is advisable to avoid using any products containing alcohol wherever possible. It is known that the smell of alcohol alone is sufficient to induce a relapse. During disulfiram treatment this could prove fatal and it is thought that a complete ban on all products containing alcohol might help to reduce this risk. If you cannot avoid using a product containing alcohol such as an antiseptic gel, try it on a small patch of skin first. If you cannot detect any symptoms after 1–2 hours, the product is almost certainly safe to use. In practice, you can only find this out through trial and error – and under the circumstances, using an alternative product is always the safest option. It is thought that a minor antabuse reaction may even prove beneficial, as the patient will get a sense of how effective the treatment is.

Overdose

A single dose exceeding 3g may cause overdose symptoms, including nausea and severe fatigue. The onset of some of the more serious symptoms may be delayed, including loss of coordination, slurred speech, and impaired cognition. Some of the symptoms may be permanent. Symptomatic treatment should be given, as there is no antidote to disulfiram. In cases of significant overdose (children 0.3g/kg, adults 0.5g/kg), disulfiram may be lethal. If you suspect a disulfiram overdose, seek emergency medical treatment or dial 112 immediately.

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