DISULFIRAM

THERAPEUTICS

Brands • Antabuse
see index for additional brand names

Generic? Yes

Class • Alcohol dependence treatment

Commonly Prescribed for (bold for FDA approved)
• Maintenance of alcohol abstinence

How the Drug Works
• Irreversibly inhibits aldehyde dehydrogenase, the enzyme involved in second-stage metabolism of alcohol
• Alcohol is metabolized to acetaldehyde, which in turn is metabolized by aldehyde dehydrogenase; thus, disulfiram blocks this second-stage metabolism
• If alcohol is consumed by a patient taking disulfiram, toxic levels of acetaldehyde build up, causing unpleasant side effects
• This aversive experience ideally leads to negative conditioning, in which patients abstain from alcohol in order to avoid the unpleasant effects

How Long Until It Works
• Disulfiram’s effects are immediate; patients should not take disulfiram until at least 12 hours after drinking

If It Works
• Increases abstinence from alcohol

If It Doesn’t Work
• Patients who drink alcohol while taking disulfiram can experience side effects, including alcohol toxicity
• Evaluate for and address contributing factors
• Consider switching to another agent

Best Augmenting Combos for Partial Response or Treatment Resistance
• Augmentation with behavioral, educational, and/or supportive therapy in groups or as

SIDE EFFECTS

How Drug Causes Side Effects
• When alcohol is consumed by a patient taking disulfiram, levels of acetaldehyde build up, causing side effects of alcohol toxicity
• One of disulfiram’s metabolites is carbon disulfide, which may be excreted through the lungs; this could account for the side effect of metallic taste

Notable Side Effects
• Metallic taste, dermatitis, sedation
• Flushing, headache, tachycardia, nausea, vomiting (if alcohol is consumed)

Life-Threatening or Dangerous Side Effects
• Hepatotoxicity
• Myocardial infarction, congestive heart failure, respiratory depression, other signs of alcohol toxicity (if alcohol is consumed)

Weight Gain
• Reported but not expected

Sedation
• Occurs in significant minority

What to Do About Side Effects
• Wait
• Reduce dose
• Take at night to reduce sedation

Best Augmenting Agents for Side Effects
• Dose reduction or switching to another agent may be more effective since most side effects cannot be improved with an augmenting agent

Tests
• Baseline and follow-up liver function tests
DISULFIRAM (continued)

**DOSSING AND USE**

**Usual Dosage Range**
- 250–500 mg/day; 1-year duration

**Dosage Forms**
- Tablet 250 mg, 500 mg scored

**How to Dose**
- The patient should not take disulfiram until at least 12 hours after drinking
- Initial 250–500 mg/day for 1–2 weeks
- Usually dosed in the morning but can be dosed at night if sedation is a problem
- Maintenance dose usually 250 mg/day; maximum dose 500 mg/day

**Dosing Tips**
- The patient must be fully informed of the disulfiram-alcohol reaction
- The patient should be advised not to consume any food or beverages containing alcohol or to use any alcohol-containing preparations (e.g., cough syrup)
- The patient should be warned that reactions may occur up to 2 weeks after disulfiram is stopped
- The patient should carry an emergency card stating that he or she is taking disulfiram

**Overdose**
- Unknown

**Long-Term Use**
- Maintenance treatment should be continued until the patient is recovered

**Habit Forming**
- No

**How to Stop**
- Taper not necessary
- A disulfiram-alcohol reaction may occur for up to 2 weeks after disulfiram is stopped

**Pharmacokinetics**
- Half-life of parent drug is 60–120 hours
- Half-life of metabolites is 13.9 hours (diethyldithiocarbamate) and 8.9 hours (carbon disulfide)

**Drug Interactions**
- Disulfiram may increase blood levels of phenytoin; baseline and follow-up levels of phenytoin should be taken
- Disulfiram may prolong prothrombin time, requiring dose adjustment of oral anticoagulants
- Use with isoniazid may lead to unsteady gait or change in mental status

**Other Warnings/Precautions**
- Disulfiram should not be given to a patient in a state of alcohol intoxication without the patient’s full knowledge
- Not recommended for patients older than age 60 or for those with severe pulmonary disease, chronic renal failure, diabetes, peripheral neuropathy, seizures, diabetes, or portal hypertension
- Use with extreme caution in patients with hypothyroidism, epilepsy, cerebral damage
- Patients taking disulfiram should not be exposed to ethylene dibromide or its vapors, as this has resulted in a higher incidence of tumors in rats

**Do Not Use**
- If the patient is in a state of alcohol intoxication
- Without the patient’s full knowledge
- For at least 12 hours after the patient last drank
- If patient is taking metronidazole, amprenavir, ritonavir, or sertraline
- If patient has psychosis
- If patient has cardiovascular disease
- If there is a proven allergy to disulfiram
- If there is a proven allergy to thiuram derivatives

**SPECIAL POPULATIONS**

**Renal Impairment**
- Not recommended for patients with chronic renal failure

**Hepatic Impairment**
- Not recommended
Cardiac Impairment
• Contraindicated

Elderly
• Not generally recommended for patients older than age 60
• Some patients may tolerate lower doses better

Breast Feeding
• Unknown if disulfiram is secreted in human breast milk, but all psychotropics assumed to be secreted in breast milk
  ❗ Recommended either to discontinue drug or bottle feed

Children and Adolescents
• Safety and efficacy have not been established

Pregnancy
• Effective June 30, 2015, the US FDA requires changes to the content and format of pregnancy and lactation information in prescription drug labels, including the elimination of the pregnancy letter categories; the Pregnancy and Lactation Labeling Rule (PLLR or final rule) applies only to prescription drugs and will be phased in gradually for drugs approved on or after June 30, 2001
• Controlled studies have not been conducted in pregnant women
• Some animal studies have shown adverse effects
• Pregnant women needing to stop drinking may consider behavioral therapy before pharmacotherapy

Potential Advantages
• Individuals who are motivated to abstain from alcohol

Potential Disadvantages
• Adherence rates can be low

Primary Target Symptoms
• Alcohol dependence

Pearls
• Some evidence of efficacy in comorbid alcohol use disorder and PTSD
• Preliminary evidence of efficacy for use in cocaine dependence, both alone and comorbid with alcohol use disorder

Suggested Reading
