ACAMPROSATE

THERAPEUTICS

Brands • Campral
see index for additional brand names

Generic? Not in USA

Class • Neuroscience-based Nomenclature: glutamate multi-modal (Glu-MM)
• Alcohol dependence treatment

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

How the Drug Works
• Theoretically reduces excitatory glutamate neurotransmission and increases inhibitory gamma-aminobutyric acid (GABA) neurotransmission
• Binds to and blocks certain glutamate receptors, including metabotropic glutamate receptors
• Because withdrawal of alcohol following chronic administration can lead to excessive glutamate activity and deficient GABA activity, acamprosate can act as “artificial alcohol” to mitigate these effects

How Long Until It Works
• Has demonstrated efficacy in trials lasting between 13 and 52 weeks

If It Works
• Increases abstinence from alcohol

If It Doesn’t Work
• Evaluate for and address contributing factors
• Consider switching to another agent
• Consider augmenting with naltrexone

Best Augmenting Combos for Partial Response or Treatment Resistance
• Naltrexone
• Augmentation therapy may be more effective than monotherapy
• Augmentation with behavioral, educational, and/or supportive therapy in groups or as an individual is probably key to successful treatment

Tests • None for healthy individuals

SIDE EFFECTS

How Drug Causes Side Effects
• Theoretically, behavioral side effects due to changes in neurotransmitter concentrations at receptors in parts of the brain and body other than those that cause therapeutic actions
• Gastrointestinal side effects may be related to large doses of a drug that is an amino acid derivative, increasing osmotic absorption in the gastrointestinal tract

Notable Side Effects
• Diarrhea, nausea
• Anxiety, depression

Life-Threatening or Dangerous Side Effects
• Suicidal ideation and behavior (suicidality)

Weight Gain
• Reported but not expected

Sedation
• Reported but not expected

What to Do About Side Effects
• Wait
• Adjust dose
• If side effects persist, discontinue use

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
ACAMPROSATE (continued)

**DOSING AND USE**

**Usual Dosage Range**
- 666 mg three times daily (>60 kg)
- 666 mg two times daily (<60 kg)

**Dosage Forms**
- Tablet 333 mg

**How to Dose**
- Patient should begin treatment as soon as possible after achieving abstinence
- Recommended dose is 666 mg three times daily; titration is not required

**Dosing Tips**
- Providing educational materials and counseling in combination with acamprosate treatment can increase the chances of success
- Patients should be advised to continue treatment even if relapse occurs and to disclose any renewed drinking
- Although absorption of acamprosate is not affected by food, it may aid adherence if patients who regularly eat three meals per day take each dose with a meal
- Adherence with three times daily dosing can be a problem; having patient focus on frequent oral dosing of drug rather than frequent drinking may be helpful in some patients

**Overdose**
- Limited available data; diarrhea

**Long-Term Use**
- Has been studied in trials up to 1 year

**Habit Forming**
- No

**How to Stop**
- Taper not necessary

**Pharmacokinetics**
- Terminal half-life 20–33 hours
- Excreted unchanged via the kidneys

**Drug Interactions**
- Does not inhibit hepatic enzymes, and thus is unlikely to affect plasma concentrations of drugs metabolized by those enzymes
- Is not hepatically metabolized and thus is unlikely to be affected by drugs that induce or inhibit hepatic enzymes
- Concomitant administration with naltrexone may increase plasma levels of acamprosate, but this does not appear to be clinically significant and dose adjustment is not recommended

**Other Warnings/Precautions**
- Monitor patients for emergence of depressed mood or suicidal ideation and behavior (suicidality)
- Use cautiously in individuals with known psychiatric illness

**Do Not Use**
- If patient has severe renal impairment
- If there is a proven allergy to acamprosate

**SPECIAL POPULATIONS**

**Renal Impairment**
- For moderate impairment, recommended dose is 333 mg three times daily
- Contraindicated in severe impairment

**Hepatic Impairment**
- Dose adjustment not generally necessary

**Cardiac Impairment**
- Limited data available

**Elderly**
- Some patients may tolerate lower doses better
- Consider monitoring renal function

**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...
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Potential Advantages
- Individuals who have recently abstained from alcohol
- For the chronic daily drinker

Potential Disadvantages
- Individuals who are not abstinent at time of treatment initiation
- For binge drinkers

Primary Target Symptoms
- Alcohol dependence

PEARLS
- Because acamprosate serves as “artificial alcohol,” it may be less effective in situations in which the individual has not yet abstained from alcohol or suffers a relapse
- Thus acamprosate may be a preferred treatment if the goal is complete abstinence, but may not be preferred if the goal is reduced-risk drinking

Labeling Rule (PLL 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
- In animal studies, acamprosate demonstrated teratogenicity in doses approximately equal to the human dose (rat studies) and in doses approximately 3 times the human dose (rabbit studies)
- Pregnant women needing to stop drinking may consider behavioral therapy before pharmacotherapy
- Not generally recommended for use during pregnancy, especially during first trimester

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

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Suggested Reading

