

## THERAPEUTICS

**Brands** • Campral

**Generic?** Yes

### Class

- Neuroscience-based Nomenclature: glutamate multimodal (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 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

## DOSING AND USE

### Usual Dosage Range

- 666 mg 3 times daily (>60 kg)
- 666 mg 2 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 3 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 3 meals per day take each dose with a meal
- Adherence with 3 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 3 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 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
- 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 are assumed to be secreted in breast milk
- Recommended either to discontinue drug or bottle feed

## **THE ART OF PSYCHOPHARMACOLOGY**

### **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



### **Suggested Reading**

Anton RF, O'Malley SS, Ciraulo DA, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. *JAMA* 2006;295(17):2003–17.

Kranzler HR, Gage A. Acamprosate efficacy in alcohol-dependent patients: summary of results

from three pivotal trials. *Am J Addictions* 2008; 17:70–6.

Rosner S, Leucht P, Soyka M. Acamprosate supports abstinence, naltrexone prevents excessive drinking: evidence from a meta-analysis with unreported outcomes. *J Psychopharmacol* 2008;22:11–23.

