# Acamprosate calcium

## THERAPEUTICS

### Brands
- Campral EC

### Generic?
Yes

### Class
- Neuroscience-based nomenclature: pharmacology domain – glutamate; mode of action – unclear
- Alcohol dependence treatment; glutamate multimodal (Glu-MM)

### Commonly Prescribed for
*(bold for BNF indication)*
- **Maintenance of abstinence in alcohol-dependence** (moderate-severe condition in combination with psychosocial interventions)

### How the Drug Works
- Theoretically reduces excitatory glutamate neurotransmission and increases gamma-aminobutyric acid (GABA) to increase abstinence
- Binds to and blocks certain glutamate receptors, including metabotropic glutamate receptors
- Acts as a functional glutamatergic NMDA antagonist
- 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
- Treatment duration of longer than 6 months suggested
- Has demonstrated efficacy in trials lasting between 13 and 52 weeks

### If It Works
- Increases continuous/cumulative abstinence from alcohol

### If It Doesn't Work
- Evaluate for and address contributing factors
- Consider switching to another agent, e.g. naltrexone or disulfiram
- Consider augmenting with naltrexone

### Best Augmenting Combos for Partial Response or Treatment Resistance
- Naltrexone
- Augmenting therapy may be more effective than monotherapy
- Use in combination with individual psychological interventions (CBT, behavioural therapy, social network/ environment-based therapies)

### Tests
- Baseline urea and electrolytes, liver function (including gamma-glutamyl transferase)
- Follow-up blood tests: liver function to check on recovery and to increase motivation

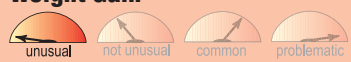
## SIDE EFFECTS

### How Drug Causes Side Effects
- Theoretically, behavioural side effects are 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
- Diarrhoea, nausea
- Anxiety, depression

**Common or very common**
- GIT: abdominal pain, diarrhoea, flatulence, nausea, vomiting
- Other: sexual dysfunction, skin reactions

### Life-Threatening or Dangerous Side Effects
- Suicidal ideation and behaviour (suicidality)

### Weight Gain


- Reported but not expected



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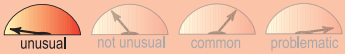
### Sedation




- Reported but not expected

### What to Do About Side Effects

- Wait
- Adjust the 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

- Adult (body weight <60 kg): 666 mg in the morning, and 333 mg at midday and at night time
- Adult (body weight ≥ 60 kg): 666 mg 3 times per day

### Dosage Forms

- Tablet 333 mg

### How to Dose

*Maintenance of abstinence in alcohol dependence:

- Patients should begin treatment as soon as possible after achieving detoxification
- Some evidence suggests can be started during detoxification for neuroprotection
- Recommended dose is 666 mg 3 times daily, titration is not required

### Dosing Tips

- Provide psychosocial intervention in combination with acamprosate treatment to increase the chances of success
- Stop if drinking persists 4 to 6 weeks after starting the drug
- Stay under supervision at least monthly for 6 months, then less frequently if taking more than 6 months
- 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 the 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

- Acute overdose can lead to persistent diarrhoea

### Long-Term Use

- Should be prescribed for 6 months or longer (licensed for 1 year)
- Has been studied in trials for up to 1 year

### Habit Forming

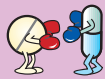
- No

### How to Stop

- Taper not necessary

### Pharmacokinetics

- Bioavailability reduced when taken with food
- Terminal half-life about 20–33 hours
- Excreted mostly unchanged via kidneys



### Drug Interactions

- Does not inhibit hepatic enzymes, and this is unlikely to affect plasma concentrations of drugs metabolised by those enzymes
- Is not hepatically metabolised 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 behaviour (suicidality)
- Use cautiously in individuals with known psychiatric illness
- Continued alcohol abuse – risk of treatment failure

### Do Not Use

- If the patient has severe renal impairment
- If the patient has severe hepatic impairment
- If there is a proven allergy to acamprosate



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## SPECIAL POPULATIONS

### Renal Impairment
- For moderate impairment, recommended dose is 333 mg 3 times per day
- Contraindicated in severe impairment

### Hepatic Impairment
- Dose adjustment not generally necessary
- Avoid in severe liver impairment

### 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
- 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 about 3 times the human dose (rabbit studies)
- Pregnant women needing to stop drinking may consider behavioural therapy before pharmacotherapy
- Not generally recommended for use during pregnancy, especially during first trimester
- Alcohol is a confirmed teratogen and therefore acamprosate use during pregnancy may be considered beneficial in some cases

### Breastfeeding
- No evidence of safety
- Long half-life increases the risk of accumulation in the breastfed infant
- Low levels anticipated in milk due to low oral absorption
- Benefit of the mother abstaining from alcohol to the infant may outweigh the risk to the infant of acamprosate

## THE ART OF PSYCHOPHARMACOLOGY

### Potential Advantages
- Individuals who have recently abstained from alcohol
- For the chronic, daily drinker
- It works as well as naltrexone for maintenance of abstinence from alcohol

### Potential Disadvantages
- Individuals who are not abstinent at time of treatment initiation
- For binge drinkers
- Naltrexone works slightly better for reducing cravings for alcohol and heavy drinking

### 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
- Studies have found that acamprosate works best when used in combination with psychosocial support since the drug facilitates a reduction in alcohol consumption as well as full abstinence
- Over 3 to 12 months it increases the number of people who do not drink at all and the number of days without alcohol
- It appears to work as well as naltrexone for maintenance of abstinence from alcohol, however, naltrexone works slightly better for reducing cravings for alcohol and heavy drinking
- Some evidence suggests that acamprosate is neuroprotective (it protects neurons from damage and death caused by the effects of alcohol withdrawal, and possibly other causes of neurotoxicity)



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## Suggested Reading

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