

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

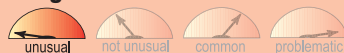
- GIT: abdominal pain, diarrhoea, flatulence, nausea, vomiting
- Other: sexual dysfunction, skin reactions



Life-Threatening or Dangerous Side Effects

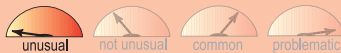
- Suicidal ideation and behaviour (suicidality)

Weight Gain



- Reported but not expected

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

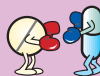
- No

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

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)



Suggested Reading

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