Criteria for Nonformulary Use of
Acamprosate (Campral®)
VHA Pharmacy Benefits Management Strategic Healthcare Group and Medical Advisory Panel

The following recommendations are based on current medical evidence and expert opinion from clinicians. The content of the document is dynamic and will be revised as new clinical data becomes available. The purpose of this document is to assist practitioners in clinical decision making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician should utilize this guidance and interpret it in the clinical context of the individual patient situation.

Refer to the National PBM Drug Monograph Acamprosate (Campral®) at http://vaww.pbm.va.gov/drugmonograph/aer8aw37AcAcamprosate%20NM.pdf or http://www.pbm.va.gov/monograph/aer8aw37AcAcamprosate%20NM.pdf. For additional resources on management alcohol use disorders, see the National Institute of Alcohol Abuse and Alcoholism Web site (http://www.niaaa.nih.gov/)

Inclusion Criteria	**Comments**
All four of the following criteria MUST be met for acamprosate to be prescribed: □ A current DSM-IV diagnosis of alcohol dependence □ Patient has had a documented insufficient response, contraindication, hypersensitivity, or intolerance to naltrexone, used in combination with any program that addresses medication adherence and provides patient education and support. □ Prior to initiation, the patient has established at least 4 days of abstinence with no more than mild alcohol withdrawal symptoms (e.g., as indicated by scores ≤ 8 on the CIWA-Ar)[1]* □ During treatment with acamprosate, the patient remains engaged in a comprehensive management program that includes a psychosocial component therapy (e.g., psychosocial behavioral interventions focused on relapse prevention)	*Please note that to date, there are too few patients in the ≥65 age group to evaluate any differences in safety or effectiveness for geriatric patients compared to younger patients.* *Please note that to date, there is no consistent evidence to suggest which types of patients may benefit from acamprosate.* [2-4] *There is insufficient evidence for the use of acamprosate in patients with concurrent illicit drug use.* *In the recently published COMBINE study,* [5-6] *no evidence of efficacy was seen when acamprosate was used alone or in combination with naltrexone. Based on this limited evidence, acamprosate is not recommended as a first-line agent, and the routine use of it in combination therapy with other antialcoholic agents including naltrexone is not recommended.* **See http://www.detoxguideline.org/ or http://vaww.mentalhealth.med.va.gov/substance_use.shtm for online training in CIWA-Ar.*[1]
Exclusion Criteria	**Comments**
€ Patients not willing to receive concomitant comprehensive management program that includes a psychosocial component therapy (e.g., psychosocial behavioral intervention focused on relapse prevention) € Severe renal impairment (CrCL ≤ 30 mL/min) € Known hypersensitivity to acamprosate calcium or any of its components	*Please Note: Acamprosate has not been established as effective for initiating abstinence in patients who have not done so prior to initiating drug therapy.* *There are no adequate and well-controlled studies in pregnant women. Acamprosate should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus. If used among women of childbearing potential, consideration of an effective contraceptive method should be discussed and recommended.* **If any of the boxes are checked in the exclusion criteria box, patient is ineligible to receive acamprosate.**
Dosing	**Comments**
Therapy should start as soon as possible after abstinence has been established and should be combined with ongoing behavioral intervention focused on relapse prevention. □ Initial dose is two 333mg acamprosate tablets (666mg) three times daily given orally. □ For patients with moderate renal impairment (creatinine clearance of 30-50 mL/min), a starting dose of one 333 mg tablet orally taken three times daily is recommended.	*Although acamprosate may be given without regard to meals, dosing with meals was employed during clinical trials and is suggested as an aid to compliance in those patients who regularly eat three meals daily.* *The pharmacokinetics of acamprosate has not been evaluated in the geriatric population.* *There are no clinical trials extending beyond 1 year with active drug therapy to substantiate the long-term efficacy of acamprosate.*

For continued use, reassessment for efficacy is needed by documenting a substantial reduction in alcohol use in the patient's medical record. The initial prescription may be written for a 30 days supply with a maximum of two refills. If the patient has established a substantial reduction in alcohol use within 90 days, then long-term treatment with multiple refills may be authorized.	
Monitoring/Patient Information	**Comments**
€ Documentation in the medical chart of patient's adherence to an ongoing comprehensive management program that includes a psychosocial behavioral intervention for relapse prevention is recommended. € Documentation in the medical chart of patient's self-report of amount and pattern of any alcohol use is recommended. € Patients, families and caregivers of patients being treated with acamprosate should be alerted to the need to monitor patients for the development of symptoms of depression or suicidal thinking, and to report such symptoms to the patient's health care provider. € Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that acamprosate therapy does not affect their ability to engage in such activities. € Documentation in the medical chart of patient's medication adherence is recommended. € Patients should be advised to continue acamprosate as directed, even in the event of relapse and to discuss any alcohol use with their provider.** € Advise female patient(s) to notify caregiver immediately if become pregnant or intend to become pregnant during therapy. € Women of childbearing potential should be instructed to use an effective contraceptive method during therapy.	*Because elderly patients are more likely to have reduced renal function, use care in dose selection; it may be useful to monitor renal function.* *There are no clinical trials extending beyond 1 year of active drug therapy to substantiate the long-term efficacy of acamprosate. Patients taking acamprosate for longer than 1 year should be reassessed on a regular basis.* *If patient has not achieved stable abstinence or clinically meaningful reduction in alcohol use after 6 weeks, assure medication adherence (e.g., with monitoring or involvement of significant other)* *** If a patient relapses while taking acamprosate, the decision to continue acamprosate should be made after weighing the potential risks versus benefits.*
Discontinuation Criteria	**Comments**
Patient is not actively engaged in a comprehensive management program that includes a psychosocial component while being prescribed acamprosate. (e.g., psychosocial behavioral interventions focused on relapse prevention) € If patient has not initially established or was not able to maintain a significant reduction in ETOH use, consider discontinuing acamprosate therapy and reevaluate the treatment plan including a more intensive level of care.	In the COMBINE trial, [5, 6] acamprosate, either alone or in combination with naltrexone, showed no advantage over placebo on any of the drinking outcome measures. Naltrexone + Medical Management (integrated treatment) resulted in better abstinence rates than acamprosate .

Approved by Physician: Date/Time

References:

1. Sullivan JT, Sykora, K, Schneiderman,J. et al. Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-AR). Br J Addiction 1989; 84:1353-1357.

2. Lesch O and Walker H. Subtypes of alcoholism and their role in therapy. Alcohol Alcohol. 1996; 31(Suppl 1):63-67.

3. Chick J, Howlett H. Morgan M et al, United Kingdom multicenter acamprosate study (UKMAS): a 6-month prospective study of acamprosate versus placebo in preventing relapse after withdrawal from alcohol. Alcohol Alcohol 2000; 35: 176-187.

4. Verheul R, Lehert P, Geerlings PG et al., Predictors of acamprosate efficacy: results from a pooled analysis of 7 European trials including 1485 alcohol-dependent patients. Psychopharmacology. 2004; 178: 167-173.

5. COMBINE Study Research Group. Pharmacotherapies and Behavioral Interventions for Alcohol Dependence. The COMBINE Study: A Randomized Controlled Trial. JAMA 2006, 295:2003-17.

6. Kranzler HR. Evidence-Based Treatments for Alcohol Dependence. New Results and New Questions. JAMA 2006; 295 :2075-76.