

CAMPRAL® (ACAMPROSATE CALCIUM) DELAYED-RELEASE TABLETS
NOVEL MEDICATION FOR THE TREATMENT OF ALCOHOL DEPENDENCE

INDICATION	Campral® (acamprosate calcium) is indicated for the maintenance of abstinence from alcohol in patients with alcohol dependence who are abstinent at treatment initiation. Treatment with Campral should be part of a comprehensive management program that includes psychosocial support. Campral is a registered trademark of Merck Santé s.a.s. subsidiary of Merck KGaA, Darmstadt, Germany.
DESCRIPTION	<p>The first new medication in nine years to be approved for the treatment of alcohol dependence, a chronic disease that accounts for approximately 100,000 deaths per year in the United States.¹</p> <p>The mechanism of action of Campral in maintenance of alcohol abstinence is not completely understood. Originally, several neurotransmitter systems, including GABA, were investigated for a possible role in Campral's mechanism of action. However, recent evidence suggests Campral's main interaction is with the glutamate system. Chronic alcohol exposure is hypothesized to alter the normal balance between neuronal excitation and inhibition. Campral is believed to act on the biochemical systems that are involved in alcohol dependence. Campral interacts with neurotransmitter systems and is hypothesized to restore the normal balance.²</p> <p>Campral's mechanism of action is different from that ascribed to currently available medications, which either block the "high" associated with alcohol³ or induce vomiting if alcohol is ingested.⁴</p>
CLINICAL BENEFITS	<p>In clinical settings and clinical practice, Campral has been proven to help up to 3 times more alcohol-dependent patients than placebo to maintain abstinence and reduce the incidence and severity of relapse.⁵</p> <p>Treatment with Campral should be part of a comprehensive management program that includes psychosocial support.⁶</p>
SAFETY	<p>Campral is safe and well tolerated.</p> <p>Campral has a low potential for drug-drug interactions and can be taken with medications commonly prescribed in this patient population, including anxiolytics, hypnotics, and sedatives (including benzodiazepines) and non-opioid analgesics.⁷</p> <p>CAMPRAL® is contraindicated in patients with severe renal impairment (creatinine clearance =30 mL/min) and requires a dose reduction in patients with moderate renal impairment (creatinine clearance of 30-50 mL/min).⁸</p> <p>In placebo-controlled trials, events related to suicide (i.e., suicide</p>

<p>FORMULATION & DOSING</p>	<p>ideation, suicide attempts) were infrequent overall, but were more common with Campral. Rates of completed suicides, however, were similar between Campral-treated and placebo-treated patients.⁹</p> <p>The recommended daily dose is two 333 mg tablets taken three times per day.¹⁰</p> <p>Treatment with Campral should be initiated as soon as possible following alcohol withdrawal and should be maintained if the patient relapses.¹¹ Medication should be used as part of a comprehensive management program that includes psychosocial support.¹²</p>
<p>SIDE EFFECTS</p>	<p>In the clinical trial program, adverse events observed during Campral treatment were generally mild with the most frequently reported adverse event being diarrhea (16% in pooled data).¹³</p> <p>In placebo controlled trials of 6 months or less, 8% of Campral treated patients discontinued due to an adverse event, as compared with 6% of patients treated with placebo.¹⁴ In studies longer than 6 months, the discontinuation rate due to adverse events was 7% in both the placebo-treated and Campral-treated patients.¹⁵</p> <p>Campral has been shown not to have addiction potential.¹⁶</p>
<p>APPROVAL</p>	<p>Campral was approved by the U.S. Food and Drug Administration (FDA) on July 29, 2004.</p> <p>FDA approval of Campral is based primarily on the Agency's review of safety and efficacy data from four double-blind, placebo-controlled trials. In three of these trials, Campral increased abstinence rates when used as part of a multidisciplinary approach that included various types of psychosocial support. In a fourth study, the Campral-treated group failed to show a difference on the primary efficacy endpoint, cumulative abstinence duration. In this trial, patients were not required to be abstinent prior to randomization as required in the positive studies.</p>
<p>CLINICAL STUDIES</p>	<p>The Campral New Drug Application (NDA) included efficacy data from four randomized, double-blind, placebo-controlled trials.</p> <p>In three of these trials, Campral increased abstinence rates when used with psychosocial support or counseling. Abstinence rates were up to 3 times higher in Campral-treated patients than in placebo-treated patients.¹⁷</p> <p>Additional parameters evaluated in the pivotal trials which demonstrated a statistically significant benefit in favor of Campral over placebo included time to first drink and percent days abstinent.¹⁸</p> <p>1. The first study of 125 patients found that 38% of patients in the</p>

<p>WHAT TO EXPECT</p> <p>MANUFACTURER</p> <p>DEVELOPMENT HISTORY</p> <p>MORE INFORMATION</p>	<p>Campral group remained continuously abstinent throughout the three month trial, versus 13% in the placebo group.¹⁹</p> <ol style="list-style-type: none"> 2. Another study of 272 patients found that 28% of Campral patients were continuously abstinent, versus 13% of those on placebo, after 48 weeks.²⁰ 3. A third, 51-week, study of 350 patients found that 16% of Campral patients remained abstinent throughout the year, versus 9% on placebo.²¹ 4. In a fourth study, the Campral-treated group failed to show a difference on the primary efficacy endpoint, cumulative abstinence duration. In this trial, patients were not required to be abstinent prior to randomization as required in the positive studies.²² <p>Clinical trials have shown that Campral significantly helps maintain abstinence in up to 3 times more alcohol dependent patients and reduces the risk of relapse compared to placebo when used in combination with psychosocial support.²³</p> <p>Forest Laboratories, Inc. markets Campral for use in the United States.</p> <p>Forest Laboratories licensed the U.S. marketing and distribution rights for Campral from Merck KGaA of Darmstadt, Germany, in October, 2001.</p> <p>The New Drug Application (NDA) was resubmitted to the FDA in December 2003. The resubmission to the FDA was based on a re-analysis of three double-blind, placebo-controlled trials that involved 998 alcohol-dependent patients. The original NDA was submitted in December, 2001.</p> <p>Visit www.Campral.com or Call 1-888-430-LABS</p> <p>FOR MORE INFORMATION ABOUT ACAMPROSATE, CONTACT:</p> <ul style="list-style-type: none"> • Media: Greg Williams (212-453-2406 or williamg@fleishman.com) • Investors: Charles E. Triano, Vice President - Investor Relations, Forest Laboratories, Inc. (212-224-6714, charles.triano@frx.com) • Professional Affairs: Kathleen Brader, (800-678-1605, extension 7301)
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- ¹ Garbutt J, M.D.; West S, PhD, MPH.; Carey T, MD, MPH.; Lohr K, PhD.; Crews F, PhD. Pharmacological Treatment of Alcohol Dependence: A Review of the Evidence. *Jama*. 1999; 281(14); 1323.
- ² CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 1.
- ³ Solhkhah R, M.D.; Wilens T, M.D. Pharmacotherapy of Adolescent Alcohol and Other Drug Use Disorders. *Alcohol Health and Research World*.1998; 22(2);122.
- ⁴ Solhkhah R, M.D.; Wilens T, M.D. Pharmacotherapy of Adolescent Alcohol and Other Drug Use Disorders. *Alcohol Health and Research World*.1998; 22(2);123.
- ⁵ Data on file, Forest Laboratories, Inc.
- ⁶ CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 4.
- ⁷ CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 6.
- ⁸ CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 5.
- ⁹ CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 5.
- ¹⁰ CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 11.
- ¹¹ CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 11.
- ¹² CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 11.
- ¹³ CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 9.
- ¹⁴ CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 8.
- ¹⁵ CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 8.
- ¹⁶ CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 11.
- ¹⁷ Data on file, Forest Laboratories, Inc.
- ¹⁸ Data on file, Forest Laboratories, Inc.
- ¹⁹ Pelc II. Acamprosate in the Treatment of Alcohol Dependence. *Brit Jrrnl of Psychiatry*. 1997; 171:73-77.
Data on file, Forest Laboratories, Inc
- ²⁰ Sass H. Relapse Prevention by Acamprosate. *Arch Gen Psychiatry*. 1996; 53:673-680.
Data on file, Forest Laboratories, Inc
- ²¹ Paille FM. Double-Blind Randomized Multicentre Trial of Acamprosate in Maintaining Abstinence from Alcohol. *Alcohol & Alcoholism* .1995; 30(2):239-247.
Data on file, Forest Laboratories, Inc
- ²² CAMPRAL[®] (acamprosate calcium) Delayed-Release Tablets Prescribing Information, Forest Laboratories, Inc., St.Louis, MO, 2004. Pg. 4.
- ²³ Data on file, Forest Laboratories, Inc.