



This drug has been "archived" and will not be actively updated except for a compelling reason or request (August 2005).

## ACAMPROSATE

### SUMMARY SHEET

**TRADE NAME: CAMPRAL EC**

#### Licensed Indications:

'Indicated as therapy to maintain abstinence in alcohol dependent patients. It should be combined with counselling'.

#### Background Information

Alcoholism is an important public health problem in Europe. Although alcohol detoxification is usually successful, maintaining abstinence proves much more difficult. Approximately 50% of alcoholic patients relapse within 3 months of completion of treatment.<sup>1</sup> Increasing the abstinence rate after acute detoxification is therefore a major goal in improving the success of treatment for alcohol dependence.

#### Mechanism of Action

Acamprosate does not have a direct effect on acute alcohol withdrawal, but is thought to reduce the 'craving' that is experienced by alcohol dependent patients. Acamprosate has a chemical structure similar to that of amino acid neurotransmitters such as gamma-amino butyric acid (GABA) and glutamate, and evidence suggests that it acts by stabilising the imbalance of neurotransmitters which is seen in alcohol dependency. Treatment should therefore be initiated promptly following alcohol withdrawal and continued for one year in conjunction with counselling. Treatment should be maintained if the patient relapses.

#### Clinical Efficacy

Three large, randomised, multicentre, double-blind, placebo-controlled, long-term studies involving over 1250 patients attending specialist centres for alcoholism have been published.<sup>1,2,3</sup> These were designed to assess the efficacy and safety of acamprosate compared with placebo over a 12 month period. In addition to trial medication, patients were given supportive psychotherapy as required, throughout the studies. To be eligible for these trials, patients had to be dependent on alcohol in accordance with DSM-III-R (Diagnostic and Statistical Manual of mental disorders: edition 3, revised) criteria, to have undergone detoxification and be abstinent.

In all three trials the percentage of patients continuously abstinent was highest in patients taking acamprosate compared to placebo at each assessment visit. At one year this difference was statistically significant in two of the three trials. The number of days of continuous abstinence (i.e. time to first relapse) was significantly greater in patients taking acamprosate compared to those taking placebo, in all three trials. The cumulative period of abstinence (i.e. the total number of days abstinent irrespective of previous drinking record) was also consistently significantly higher in patients taking acamprosate compared to placebo.<sup>1,2,3</sup>

Although a high percentage (50-60%) of patients had withdrawn from the trials after one year, acamprosate appeared to induce an improvement in the duration of patient follow-up. This may be of importance as the duration of follow-up is considered to be of prognostic value.

Treatment was continued for one year after which active treatment was discontinued and patients were followed up for a further 6<sup>2</sup> to 12<sup>1,3</sup> months. After this follow-up period, results from the trials become somewhat inconsistent, possibly due to the large number of patient withdrawals. However, in the two trials in which patients were followed for a further 12 months without active treatment, the difference between the two groups in the percentage of patients remaining continuously abstinent was still statistically significant.<sup>1,3</sup>

## Adverse Effects

Acamprosate proved to be generally well tolerated during clinical trials. Adverse events were mostly seen early in treatment and were usually mild and transient in nature. Due to the complex nature of alcohol dependence and symptoms of withdrawal, it may be difficult to distinguish adverse drug reactions from alcohol-related symptoms. Adverse events which were significantly more frequent in patients taking acamprosate than in placebo patients were diarrhoea (15%) abdominal pain (3.7%) 'pins and needles' in limbs (7.0%), confusion (1.7%), decreased libido (9.1%), frigidity or impotence (4.3%) and increased libido (2.5%).<sup>4</sup> Also noted were pruritus, occasional maculopapular rash and rare cases of bulbous skin reactions.<sup>5</sup> No adverse events were noted on abrupt withdrawal of acamprosate after one year, no interaction with alcohol was seen and there was no evidence of addiction to the drug.

## Health Economics

At current prices, the cost for one year of treatment with Campral EC is approximately:

- for a patient > 60kg (2 tablets tds) = £650.50
- for a patient < 60kg( 2 tablets o.m.; 1 tablet at noon; 1 tablet o.n.) = £433.70

## Summary

In three well designed trials, acamprosate has been shown to be significantly more effective than placebo at maintaining abstinence, increasing the time to first relapse and increasing the total cumulative period of abstinence in alcohol dependent patients over a one year treatment period. Trials have only been undertaken over a one year treatment period and there is no evidence for the effect of continuing treatment beyond this time.

Acamprosate does not directly affect withdrawal but should be initiated promptly afterwards, in conjunction with counselling. Treatment should be continued for a period of one year and should be maintained if the patient relapses.

Patient selection is important and the role of acamprosate appears to be in those patients who have not previously been able to change their behaviour. Patients should show a commitment to remaining abstinent and treatment should be taken in conjunction with counselling or support group attendance.

## References

1. Whitworth AB, Fischer F, Lesch OM, Nimmerrichter A, Oberbauer H, Platz T, Potgieter A, Water H and Fleischhacker WW. Comparison of acamprosate and placebo and long-term treatment of alcohol dependence. *Lancet* 1996; 347:1438-1442
2. Paille FM, Guelf JD, Perkins AC, Royer RJ, Steru S and Parot P. Double-blind randomized multicentre trial of acamprosate in maintaining abstinence from alcohol. *Alcohol and Alcoholism*, 1995; 30(2): 239-247
3. Sass H, Soyka M, Mann & Zieglgänsberger W. Relapse prevention by acamprosate: Results from a placebo-controlled study on alcohol dependence. *Arch Gen Psychiatry*, 1996; 53: 673-680
4. Anon. Campral (Acamprosate) in the treatment of alcoholism: monograph. *Group Lipha*. France 1996
5. Anon. Campral ED: Summary of Product Characteristics. *Lipha Pharmaceuticals Ltd*. December 1995.

