A.1	Acamprosate – alcohol use disorder – EML
Draft recommendation	☒ Recommended ☐ Not recommended **Justification**: Based on all available data in the public domain, in treatment for alcohol use disorders, ACAMPROSATE has been found to be slightly more efficacious in promoting abstinence.
Does the proposed medicine address a relevant public health need?	☒ Yes ☐ No ☐ Not applicable **Comments:** Alcohol is a psychoactive substance that poses health risks, and the extent and effects of these risks vary widely among consumers. Repeated drinking can lead to alcohol dependence, which is manifested by poorly controlled drinking. The concept of "harmful" use of alcohol, introduced in 2010, represents the consumption of alcohol that leads to harmful health and social consequences for the drinker and those around him. Alcohol use represents a significant social and public health burden worldwide. Five percent of the world's adult population suffers from alcohol use disorders, and alcohol dependence affects 2.6 percent of adults worldwide, or 144 million people. Mortality attributable to alcohol use is higher than that attributable to diseases such as tuberculosis, HIV/AIDS and diabetes. In 2016, alcohol use led to approximately 3 million deaths worldwide (5.3% of all deaths), of which 2.7 million were among men. Young people are disproportionately affected by alcohol use; among 20-39 year olds, 13.5% of all deaths were attributed to alcohol. Alcohol is estimated to reduce life expectancy by 0.9 years over the next 30 years. Alcohol dependence is among the main leading health risk factors in most developed and developing countries. There is a WHO global alcohol action plan 2022-2030 to reduce the harmful use of alcohol. Therapeutic success of psychosocial programs for relapse prevention is moderate, but could potentially be increased by adjuvant treatment. Pharmacologically controlled drinking in the treatment of patients suffering from alcohol dependence or alcohol use disorders is an emerging concept.

Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication? (this may be evidence included in the application, and/or additional evidence identified during the review process)	☒ Yes ☐ No ☐ Not applicable **Comments**: Acamprosate is a calcium salt of N-acetylhomotaurine and has had approvals for post-withdrawal maintenance of alcohol abstinence. Acamprosate has been proven to reduce heavy drinking and maintain abstinence once someone is already sober. It can also help manage cravings in some people. Acamprosate appears to be an effective and safe treatment strategy for supporting continuous abstinence after detoxification in alcohol dependent patients. Even though the sizes of treatment effects appear to be rather moderate in their magnitude, they should be valued against the background of the relapsing nature of alcoholism and the limited therapeutic options currently available for its treatment. A meta-analysis of 27 randomized controlled trials of acamprosate (6 to 12 months) found that acamprosate was significantly more likely than placebo treatment to prevent the resumption of alcohol use. This finding replicates the results of a previous meta-analysis using the individual records of more than 6,000 participants in 22 acamprosate studies, which found that the drug provided a significant gain in the rate of complete abstinence and freedom from binge drinking during the study period. Post-treatment follow-up studies have shown that the effects of acamprosate are maintained for up to one year after the last dose. Combining evidence-based pharmacological and behavioral treatments for AUD may increase the likelihood of individuals with AUD meeting their goals for recovery.
Does adequate evidence exist for the safety/harms associated with the proposed medicine? (this may be evidence included in the application, and/or additional evidence identified during the review process)	☒ Yes ☐ No ☐ Not applicable **Comments**: Acamprosate is not metabolized by the liver and is not associated with hepatotoxicity. It does not interact with medications commonly prescribed, including antidepressants, anxiolytics, or hypnotics. Pharmacokinetic studies found that coadministration with naltrexone increased the rate and extent of acamprosate absorption without compromising its tolerability. Acamprosate is well tolerated with minimal side effects (mild to moderate diarrhea).
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments:
Are there any special requirements for the safe, effective and appropriate use of the medicines? (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☐ Yes ☒ No ☐ Not applicable Comments:

Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	☒ Yes ☐ No ☐ Not applicable **Comments**: Acamprosate would be cost-effective. Cost-effectiveness should include the reduction in societal costs of harmful alcohol use (arrests, traffic accidents, employment). For reference, the NICE guideline developed an economic model to assess the cost-effectiveness of pharmacological therapies for relapse prevention in people in recovery from alcohol dependence. They found that the incremental cost-effectiveness of acamprosate compared with standard care was within the cost-effectiveness
Are there any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☐ No ☐ Not applicable Comments:
Is the proposed medicine recommended for use in a current WHO guideline? (refer to: https://www.who.int/publications/who-guidelines)	☐ Yes ☐ No ☐ Not applicable **Comments**: The 2016 WHO mhGAP Intervention Guide for Mental, Neurological and Substance Use Disorders in Non-Specialized Health Settings recommends considering pharmacologic intervention to prevent relapse in alcohol dependence, including acamprosate, naltrexone and disulfiram.