

Please find below the comments from the Department of Mental Health and Substance Use on the Application “A.26 Naltrexone” for updating the 2021 Model List of Essential Medicines (EML).

Application number	A.26 – Naltrexone
Name of the application	Application to add naltrexone to the WHO Model List of Essential Medicines
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Date of submission	

Alcohol use disorders are common health conditions associated with significant health and social consequences. According to the latest (2016) WHO estimates, globally 283 million people aged 15+ years live with alcohol use disorders (or 5.1% of world population aged 15+). The past 12-month prevalence of alcohol dependence (the most severe form of alcohol use disorders) is estimated as 2.6% among people aged 15+ years (WHO, 2018).

Alcohol use disorders are associated with high levels and detrimental patterns of alcohol consumption that are causally linked to multiple other health conditions such as liver diseases, some types of mental disorders and cancers, intentional and unintentional injuries. Overall, alcohol-attributable disease burden worldwide is unacceptably high and in 2016 estimated to be around 5% of all deaths and DALYs worldwide (WHO, 2018) .

Treatment of alcohol use disorders is an important component of societal responses to alcohol-related health and social problems. WHO Global strategy to reduce the harmful use of alcohol (WHO, 2010) calls for “increasing capacity of health and social welfare systems to deliver prevention, treatment and care for alcohol-use and alcohol-induced disorders and co-morbid conditions” and affirms that health services “should provide prevention and treatment interventions to individuals and families at risk of, or affected by, alcohol-use disorders and associated conditions”. One of the operational objectives of the global alcohol action plan 2022-2030 adopted by 75th World Health Assembly (2022) includes the task of enhancing “treatment capacity of health and social care systems for disorders due to alcohol use and associated health conditions as an integral part of universal health coverage...”. In its proposed actions for Member States the action plan calls for “the assurance of universal access to affordable treatment and care for people with alcohol use disorders within national health systems” (WHO, 2023). Finally, the SDG 2030 agenda in its health target 3.5 calls for strengthening prevention and treatment of substance abuse and includes coverage of pharmacological interventions in one of its two indicators (UN, 2016).

Currently the WHO Model List of Essential Medicines does not include medications for the treatment of alcohol use disorders, though three medications (acamprosate, disulfiram and naltrexone) are included in the published WHO guidelines referenced in the text of the application (WHO, 2017). At the same time the treatment coverage for alcohol use disorders, including alcohol dependence, is very low (Mekonen et al, 2021). Hence, in view of the above, the application to include naltrexone on the WHO Model List of Essential Medicines is timely and in line with the overall guidance provided by the above-mentioned global policy frameworks and action plans.

The application includes two formulations of naltrexone for treatment of alcohol use disorders/alcohol dependence: 50 mg oral tablets and 380 mg extended-release formulation.

With regards to the 50 mg oral tablets formulation, the application provides a comprehensive overview of data on effectiveness, cost-effectiveness and safety of naltrexone in management of alcohol use disorders. The data presented and referenced in the application, including positive treatment outcomes in particular groups of people with alcohol use disorders, is in line with information from other sources on safety profile of naltrexone (Bolton et al., 2019) and its effects depending on phenotype heterogeneity (Ray et al., 2019; Hartwell et al., 2020). Naltrexone is included in WHO guidelines for management of alcohol use disorders in non-specialized health settings (WHO, 2017), included in many national guidelines, for example, recommended for maintaining abstinence in treatment of alcohol dependence in Australian guidelines for the treatment of alcohol problems (Haber et al, 2021).

The information presented in the application points towards feasibility of inclusion of oral naltrexone in the menu of treatment options for alcohol use disorders in less-resourced countries.

With regards to the 380 mg extended-release formulation, the application provides data in support of effectiveness and safety of this naltrexone formulation, but it is less studied and substantially more expensive in comparison with oral tablet formulation. Very limited information is available on the use of extended-release formulations of naltrexone in low- and middle-income countries, and currently there are no studies directly comparing oral and extended-release formulations of naltrexone for treatment of alcohol use disorders.

In consideration of the proposal to include naltrexone in the WHO Model List of Essential Medicines it is important to mention that naltrexone is used for treatment of another health condition that has a significant public health impact, namely – opioid dependence. Naltrexone is recommended for relapse prevention in WHO Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence (WHO, 2009) and included in WHO/UNODC International Standards for the Treatment of Drug Use Disorders (WHO/UNODC, 2020) and many national guidelines for treatment of opioid use disorders.

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