F.7	Nicotine replacement therapy – lozenges and mouth spray – EML
Draft recommendation	☐ Recommended ☐ Not recommended **Justification:** Smoking is considered an epidemic, indeed, one of the most important public health problems worldwide. It is also the most significant preventable cause of death, of a high number of premature deaths, and avoidable chronic diseases. According to the World Health Organization (WHO) Framework Convention for Tobacco Control (FCTC), tobacco cessation is a primary health care service that should be provided not only to the people having adverse habits of consuming tobacco but also to the non-consumer, as they can also be harmed due to its deleterious effects. Therefore, 181 countries have signed this convention. Current standard for smoking cessation is a combined psychological and pharmacological treatment. Approximately 70% of people who smoke cigarettes want to quit smoking. Various aids of achieving cessation have been studied, including education of the ill effects of tobacco to the patient, behavioural counselling, and pharmacotherapy. Various pharmacological interventions are available nowadays but nicotine replacement therapy (NRT) is most widely used. The various types of NRT products results in general and breakthrough craving relief with immediate release of nicotine. All of these products have different levels of efficacy and variable rates of nicotine absorption. Combining a nicotine patch with other NRT products is more effective than use of a single product. Including various new forms of NTR would enrich the personalized options for help people to quit smoking.
Does the proposed medicine address a relevant public health need?	☒ Yes ☐ No ☐ Not applicable **Comments:** If they stopped smoking, smokers could reduce their risk of tobacco-related morbidity and mortality and potentially gain up to 10 years of life. Smoking is the most significant modifiable risk factor of morbidity and mortality, associated with a wide range of diseases. Smoking-related illnesses are estimated to cause more than 8 million deaths annually, worldwide. More deaths are attributed to cigarette smoking each year than to any other preventable cause. Recent population-based studies showed that prolonged smoking was associated with 10 years reduced life expectancy, and cessation before the age of 40 reduced the risk of smoking-related death by up to 90%. Evidence suggests that approximately half of the smokers reported having made a quit attempt in the past year, but less than 10% of such attempts succeed.

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:** Tobacco use is a chronic disorder sustained by physical dependence on nicotine and learned behaviors. Behavioral counselling and pharmacotherapy, with NRT, varenicline or bupropion, are effective treatments when used individually, but are even more effective when used in combination. In a meta-analysis, the combination of medication and behavioral counselling was associated with a 6-month quit rate of 15.2%, compared with 8.6% with brief counselling or usual care. The EAGLES trial, a double-blind randomized clinical trial, directly compared the efficacy and safety of varenicline, bupropion, the nicotine patch, and placebo and found a significantly higher 6-month quit rate for varenicline (21.8%) than for bupropion (16.2%) and the nicotine patch (15.7%). Each therapy was more effective than placebo (9.4%). A 2018 Cochrane review found high-quality evidence that all licensed forms of NRT (gum, transdermal patch, nasal spray, inhaler, and sublingual tablets or lozenges) can help people who are trying to quit increase their chances of successfully quitting smoking. NRTs increase cessation rates by 50-60% in any setting, and it is highly unlikely that additional research will change our confidence in the effect estimate. Nicotine lozenges can replace nicotine gum in patients who require intermittent, controlled doses of nicotine but are unable to chew them for a prolonged period. Studies have shown that the amount of nicotine absorbed per lozenge appears to be slightly higher than that delivered by gum. The advantage of nicotine lozenges is that they are easy to use and the taste is acceptable to the patient. However, the patient should be advised not to eat or drink 15 minutes before or during use and not to swallow or chew excessively during consumption. Researchers studied both mint and nicotine lozenges and concluded that the 4 mg nicotine lozenges significantly improved smoking cessation rates. The nicotine inhaler can be sprayed into the mouth (without being inhaled or swallowed for a few seconds) and is mainly used by patients when they feel like smoking. The rate of absorption through the inhaler is the same as that of nicotine gum, which occurs primarily through the oral mucosa. A study has shown that the use of oral nicotine inhalers can result in a long-term reduction in smoking over a 24-month period. It has been estimated that the use of different forms of NRT resulted in more adequate nicotine replacement from various mechanisms, possibly generating additive effects (patch releases steady-state nicotine serum level to prevent acute withdrawal, while another NRT form, like gum/lozenge, sprays may provide a coping mechanism addressing the behavioral urge of smoking).
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: NRT often causes minor irritation of the site through which it is administered, and in rare cases can cause non-severe chest pain and palpitations.

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: The availability of various modalities of NRT varies from country to country, and these tobacco cessation measures are poorly implemented, especially in low- and middle-income countries. Among the 1.3 billion tobacco users in the world, 70% do not have access to comprehensive tobacco cessation services.
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: Nicotine replacement therapy in the form of gum and transdermal patches has been included on the WHO Model List of Essential Medicines since 2009.