

To: WHO Expert Committee on the Selection and Use of Essential Medicines

Re: The inclusion of cytisine on the WHO Model List of Essential Medicines (EML) for the treatment of nicotine dependence as an aid to stopping smoking and tobacco use

Madrid, October 29th, 2024

Nofumadores.org, Spanish NGO, welcomes the review of cytisine to be included on the WHO Model List of Essential Medicines (EML) for the treatment of nicotine dependence as an aid to stopping smoking and tobacco use.

Tobacco smoking remains among the leading causes of preventable death and disease worldwide and is a major global public health challenge. According to WHO estimates, there are 1.3 billion tobacco users worldwide and over 80% of them live in low- and middle-income countries. While the smoking prevalence has been decreasing worldwide, the average global smoking rate remains unacceptably high and approximately 8 million people continue to die every year from smoking related diseases.

Nicotine is a highly psychoactive substance and contributes to chronic and long-term tobacco addiction, also among teenagers. Smoking by pregnant women increases the risk of nicotine addiction among children and may contribute to epigenetic outcomes. Smoking increases the risk of developing cancer, cardiovascular disease, chronic obstructive pulmonary disease (COPD) and tens of other diseases and health conditions, including infectious diseases such as tuberculosis. Smokers infected by HIV or SARS-CoV-2 are at higher risk for severe disease and death compared to non-smokers. Cigarette smoking causes premature death. Life expectancy for smokers is at least 10 years shorter than for non-smokers. *Half of all regular cigarette smokers will eventually be killed by their addiction.*

There are immediate and long-term health benefits in quitting for all tobacco users. Smoking cessation at age 50 halves the risk of premature death and cessation at age 30 reduces the risk to the level observed for never smokers. Ten years after quitting smoking, the risk of developing lung cancer is 50% lower compared to people who continue to smoke, and after 15 years of quitting, the risk of developing CVD is almost comparable to someone who has never smoked. There are also short-term benefits to health that occur only few hours, weeks or months following smoking cessation, such as eliminating the exposure to such toxic chemical compounds as tobacco smoke derived carbon monoxide, reduced frequency of cough and shortness of breath, as well as improved circulation and lung function.

Global targets for tobacco use will not be reached unless current tobacco users quit. In fact, many tobacco users report that they want to quit. According to the Global Adult Tobacco Survey (GATS), over 60% of smokers indicated that they intend to quit, and over 40% had attempted to quit in the past 12 months. Yet, without medications or cessation support, only about 4% of attempts to quit tobacco will succeed given highly addictive nature of nicotine. There is an increasing consensus that tobacco dependence is a disease that must be treated by healthcare professionals through a combination of evidence-based cessation medications and behavioral counseling.

Moreover, smoking cessation is one of the main strategies suggested by the WHO's MPOWER package against the tobacco epidemic. The WHO FCTC Article 14 and its implementation guidelines call on its Parties to "facilitate accessibility and affordability for treatment of tobacco dependence". However, the "WHO report on the global tobacco epidemic 2019: offer help to quit tobacco use" shows that cessation policies are still among the least implemented of all WHO FCTC demand reduction measures, with only 23 countries in total providing best-practice cessation services, the majority of which are high income countries. There is a room for greater action and adding cytisine on the WHO EML, medicines that satisfy priority healthcare needs to which people should have access at all times in sufficient amounts, has the potential to act as a catalyst for further sustainable tobacco control measures at global and national levels.

Cytisine is a plant-derived alkaloid found in the so-called Golden Rain (*Laburnum anagyroides*) and other members of the *Fabaceae* family. It is the oldest medicine used in smoking cessation, in Central and Eastern Europe since the mid-1960s. Like varenicline, cytisine is structurally similar to nicotine and acts as a partial agonist at nAChRs, although the medications have different half-lives and dosing regimens. It effectively inhibits nicotine from binding to nAChRs and reduces the reward obtained from tobacco consumption. Results of clinical trials and systematic reviews and meta-analyses of clinical studies indicates on high efficacy of cytisine as smoking cessation aid (comparable with varenicline, evaluated to be the most effective pharmacotherapy for smoking cessation), its high cost-effectiveness (cytisine is the cheapest smoking cessation medicine, few times cheaper than NRT and bupropion) and safety (adverse reactions to cytisine are moderate, non-serious, self-limiting and less frequent than in patients using other smoking cessation medicines).

As evaluated by group of high-level experts in their statement sent to the 23rd WHO Expert Committee on the Selection and Use of Essential Medicines (see attached document), cytisine appears to be "...effective, cost-effective, safe, affordable, practicable, acceptable and equitable". The clinical and economic characteristics of cytisine indicate that this smoking cessation aid seems to be promising for strengthening smoking cessation efforts and increasing tobacco use quit rates at global scale, but especially in low- and middle-income countries where the tobacco use epidemic and health burden from tobacco use has grown in past decades.

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Nofumadores.org strongly believe that access to evidence-based smoking cessation medication is a key component of a comprehensive, integrated tobacco control program. Offering tobacco users assistance in their cessation efforts will reinforce other tobacco control policies by increasing support for them and enhancing their acceptability. Effective cessation interventions save lives.

Therefore, [name of organization or institution] strongly supports the inclusion of cytisine on the WHO EML for the treatment of nicotine dependence as an aid to stopping smoking and tobacco use.

Thank you for your time and consideration,

Raquel Fernández Megina
President of Nofumadores.org