Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: *Nicotine Dependence (E-cigarettes)*
-July 2020-

Background:

During the Summer 2020 Meeting, the IHS National Pharmacy and Therapeutics Committee (NPTC) reviewed nicotine dependence, electronic nicotine delivery systems (ENDS) and FDA-approved cessation medications. The NPTC last reviewed these medications in August 2015. Tobacco use continues to be the primary preventable cause of death and disability in the United States and among American Indian /Alaska Native (AI/AN) people. The IHS National Core Formulary includes all seven FDA-approved medications for nicotine dependence, including five forms of nicotine replacement therapy (NRT), bupropion, and varenicline. After careful review of recent studies and system-wide utilization of these medications, **no changes were made to the National Core Formulary (NCF)**.

Discussion:

Thirty-four million American adults smoke daily. Most start during adolescence. Two-thirds of smokers want to quit and most require multiple attempts before success. More than two-thirds of adult smokers attempt to quit with achieve a success rate of approximately 8% (without evidence-based treatment) while relapse rates exceed 50%. U.S. annual healthcare costs associated with smoking exceed $170 billion.[1] While smoking prevalence overall is down to ~14%, AI/ANs have a prevalence rate of 35% which represents the highest of any ethnic group in the U.S. Currently, the leading cause of death for AI/ANs is cardiovascular disease. Meanwhile, lung cancer is the leading cause of cancer-related death in Indian Country. Both illnesses are directly impacted by tobacco use.[2]

Nicotine is known to be as addictive as heroin and cocaine. Nicotine dependence is a chronic relapsing disease that should be addressed at every patient encounter by asking the patient if they smoke, and if so, if they would like to quit. Current clinical guidelines recommend offering behavioral therapy along with pharmacotherapy to facilitate cessation in people who smoke >10 cigarettes daily. There is an absence of quality evidence about whether medications help light smokers or non-daily smokers. Single modality treatment with behavioral counseling is recommended for these patients. Behavioral counseling alone is also recommended for pregnant and adolescent patients who desire smoking cessation because of potential adverse medication risks.[3] Outside referral services such as 800-QUIT-NOW (800-784-8669) and websites, including smokefree.gov, are available when local resources are lacking.

A review of current systematic reviews and meta-analyses indicates that while ENDS, such as electronic-cigarettes, may have a potential place in cessation treatments[4], the evidence is insufficient to recommend[5,6] e-cigarettes for the treatment of nicotine dependence. Any potential benefit to adult smokers would require complete substitution of ENDS for combustible tobacco products to accomplish harm reduction. Studies comparing patients using NRT (single agent) with e-cigarettes demonstrate a 1-year abstinence rate of 18.0% vs. 9.9%, favoring e-cigarettes (relative risk, 1.83; 95% CI: 1.30 to 2.58; $p<0.001$).[7] However, at 52 weeks, continued e-cigarette use in the "abstinent use group" was 80% (63 of 79 participants) vs. 9% (4 of 44 participants) in the NRT use group, indicating greater continued nicotine dependence with e-cigarettes.

The use of "dual" or "poly" products (using more than one tobacco product) is associated with heavier tobacco use and greater nicotine dependence, leading to decreased cessation success.[8] E-cigarette poly users are more likely to be younger than age 25.[9-11] ***Notably, the newer 4th generation e-cigarettes appear designed to recruit new teenage smokers, which threatens the success in smoking cessation in recent years and may lead to a new generation of nicotine dependence.***[12,13]

Combination NRT therapy (nicotine patch + short-acting NRT), starting with a 21mg patch and a short-acting NRT based on patient preference, produces the best cessation results for NRT therapy (comparable to varenicline).[14] It is the most cost-effective of the options currently available. The NRT nasal spray and inhaler are the least tolerated of the available short-acting NRT options.[15] Abnormal dreams represent the most common adverse event. Removing the nicotine patch at bedtime often helps resolve this issue for patients.

Varenicline remains the most effective single agent for cessation vs. placebo (RR 2.24, 95% CI: 2.06 to 2.43).[16] There is also benefit with extending therapy from 12 to 24 weeks for some patients. Nausea is the most common side effect reported. In heavy smokers, adding bupropion to varenicline results in greater cessation at 6 months, but that benefit is lost at 1 year. A 2008 meta-analysis showed that varenicline resulted in similar 6-month, post-quit abstinence rates when compared to combination NRT (33.2% vs 36.5%). Of interest, the post-quit rate for nicotine patches (alone) was 23.4% (95% CI: 21.3 to 25.8)[3].

Bupropion (RR 1.64, 95% CI: 1.52 to 1.77) and single NRT therapy (RR 1.55, 95% CI: 1.49 to 1.61) demonstrate similar benefit when compared with placebo.[17] Extending bupropion therapy for 52 weeks has been shown to lead to higher abstinence rates, up to 1.5 years, although this benefit reportedly disappears by 2 years.[18] Neuropsychiatric risks such as suicidal ideation are greater with bupropion than with other cessation options, especially in adults aged 24 years and younger. Insomnia is the most common adverse event.[19] Evidence is insufficient to recommend combining bupropion and NRT.

Nortriptyline and clonidine are not FDA-approved tobacco cessation medications. They remain second-line agents with limited efficacy in tobacco cessation, while the adverse effects of these medications generally preclude their routine use.

Behavioral counseling for tobacco cessation is as efficacious as single NRT or bupropion. In general, the combination of any nicotine-cessation medication regimen increases quit rates by at least 10-20%.

Findings:

Nicotine dependence is a chronic relapsing disease that should be addressed at every primary care visit using evidence-based models ("5 A's") for brief cessation by Asking about tobacco use, Advising to quit, Assessing willingness to quit, Assisting by offering counseling with FDA approved medication, and Arranging follow up. Pregnant women, adolescents and light smokers should be offered behavioral intervention alone. Determining patient preference for cessation medication is preferred. Combination nicotine replacement therapy (patch + short-acting agent) and varenicline are first-line therapies. Bupropion and other medication combinations can be offered as needed. While e-cigarettes have been shown to decrease combustible tobacco use, they do not have a place in cessation treatment at this time.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

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