Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Nicotine Dependence***
-October 2023-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) reviewed more recent evidence since the last review of electronic nicotine devices and FDA-approved pharmacotherapy and for nicotine dependence in July 2020. Currently, the IHS National Core Formulary includes all seven FDA-approved medications for nicotine dependence including bupropion, varenicline and five forms of nicotine replacement therapy (NRT). After careful review of clinical studies, the NPTC made **no modifications** to the National Core Formulary.

Discussion:

Commercial tobacco use particularly in the form of combustible cigarettes is the leading cause of preventable disease, disability, and death among adults in the United States[1,2] An estimated 34 million U.S. adults currently smoke, and more than 1 in 5 American Indian/Alaska Native adults smoke commercial cigarettes.[1,3] Over 3 million U.S. youth reported using a commercial tobacco product, which is approximately one in six high school students and one in twenty-two middle school students; thirty-one percent reported using two or more tobacco products.[4] Though combustible cigarette use has been declining in youth, those ages 12 to 17 years overwhelmingly prefer nicotine vaping[4], and cigars were the most commonly used combustible tobacco product.[5]

The U.S. Preventive Services Task Force recommends with high certainty that clinical staff screen all adults including pregnant women for tobacco use regardless of the presence or absence of risk factors, and that if a positive screen has been identified, intervention and counseling should be offered.[6] Utilization of brief intervention approaches for all ages such as the 5A's (Ask, Advise, Assess, Assist, and Arrange) or an abbreviated version of 2A's and R (Ask, Advise, Refer) should be offered at each visit.[1,3,6,7]

Commercial tobacco intervention should account for both the physiological aspects of nicotine dependence through the use of FDA-approved pharmacotherapy for those who smoke >10 cigarettes/day and behavioral habits through behavior change counseling, of which telephone quit lines have been shown to be efficacious. [6-8]

Interventions for pregnant women and adolescents remain focused on behavioral counseling.[6] Pharmacotherapy has been shown to be ineffective for use in adolescents and is not recommended.[6,9] Current evidence is inconclusive regarding the use of NRTs and do not support the use of sustained release bupropion and varenicline in these specific groups.[9] One review found there was a moderate level of evidence that NRTs were more effective than placebo or behavioral therapy in maintaining abstinence during pregnancy (OR 1.37, 95% CI: 1.08-1.74, I^2=34%) but this was not observed at 12 months (OR 1.04, 95% CI: 0.57-1.88), leading to the conclusion that clinicians may consider NRTs only if behavioral interventions are not successful in pregnant women.[9]

Nicotine bioavailability can be characterized on a spectrum dependent on pH level where the more acidic the product, the greater its bioavailability.[10] Nicotine salt products (e.g., 4th generation e-cigarette and vaping pods) being the most acidic allow for higher levels of nicotine to be inhaled with less throat irritation, making it more user-friendly versus combustible cigarettes, which are composed of freebase nicotine that is more alkaline.[10] One pack of commercial cigarettes may contain up to 22mg of nicotine whereas the more evolved ELFBAR electronic vaping devices contains about 650 mg of nicotine, or roughly the equivalent of 590 cigarettes.[11] This is particularly concerning as people <25 years old are more likely to use e-cigarettes or vapes, possibly due to intense targeted advertising campaigns.[5]

A Cochrane review reported higher 6-month quit rates from smoking with e-cigarettes containing nicotine when compared to single NRT (RR 1.62, 95% CI: 1.3 to 2.04, p<0.0001) and e-cigarettes containing no nicotine (RR 1.94, 95% CI: 1.21 to 3.13, p= 0.006).[12] Another recent meta-analysis and systematic review showed a positive association with e-cigarette use and smoking cessation (OR 1.78, 95% CI: 1.41 to 2.25, p<0.00001), but the strength of evidence was low due to risk of bias, inconsistency of studies, lack of blinding, and short follow-up time.[13] In a 2021 AHRQ review, higher smoking quit rates were seen among e-cigarettes users (11%) vs. non-e-cigarette users (4%) at 12-months of follow-up (p=0.04), but 27% of those who quit smoking continued to use e-cigarettes after 1 year.[14] The CDC states that e-cigarettes have the potential to benefit adults who smoke, but considers them unsafe for youth, pregnant people and those who did not already use tobacco products.[3,15] Overall, current evidence remains inconclusive on their efficacy and safety.

The American Thoracic Society lists several strong recommendations based on moderate certainty of evidence for the use of varenicline over NRT and bupropion for initial treatment of adults and patients with comorbid psychiatric conditions,

and endorses extended duration therapy (>12 weeks) over standard duration therapy of 12 weeks.[17] It is important to note that some of the American Thoracic Society authors also serve on the Pfizer Advisory Committee.[17] Though the data is conflicting[16,19], it does suggest that extending varenicline duration to 24 weeks may be effective in attaining higher abstinence rates.[16,20] Varenicline continues to show greater quit rates compared to NRT monotherapy and bupropion sustained release[14,17] and when combined with NRT, there is moderate quality of evidence that it is more effective. It was not shown however to be superior to combination NRT.[17]

Combination NRT starting with higher strengths of the patch and short-acting NRT continue to show greater quit rates[21] without being associated with more adverse events or severe adverse events.[16] However, extended duration of therapy did not show improved quit rates.[21]

Findings:

As with the 2020 NPTC review, this review confirms the high level of evidence supporting combination therapy in conjunction with behavioral interventions.[14] Combination therapy increases quit rates by 68-98% compared with minimal or no treatment. The combination therapy best suited for the patient must account for the spectrum of recovery which includes high relapse rates, especially with higher levels of nicotine dependence.[14] Extending duration of treatment may improve abstinence rates but cost may be a barrier.

Electronic nicotine cigarettes may assist with quitting commercial cigarettes, but evidence suggests such abstinence does not translate to overall nicotine cessation, and these products are not FDA-approved as cessation aids. At this time, second-line agents (e.g., nortriptyline and clonidine) which were reviewed by NPTC in July 2020 do not show further evidence to be considered as first-line therapy.

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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