



February 7, 2018

Leslie Kux, Associate Commissioner for Policy  
Dockets Management Staff (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Rm. 1061  
Rockville, MD 20852

Re: Approach to Evaluating Nicotine Replacement Therapies

Dear Associate Commissioner Kux:

On behalf of the American Academy of Family Physicians (AAFP), which represents 129,000 family physicians and medical students across the country, I write in response to the request for comments titled, "Approach to Evaluating Nicotine Replacement Therapies" as published by the Food and Drug Administration (FDA) in the November 30, 2017 *Federal Register*.<sup>1</sup>

In general, the AAFP believes over-the-counter (OTC) nicotine replacement products (NRT) are much more effective in smoking cessation when accompanied by counseling, a point noted in the U.S. Public Health Service guidelines, "Treating Tobacco Use and Dependence: 2008 Update," and reinforced in the literature over the decade since then.<sup>2</sup>

Though not explicitly addressed in this FDA request for comments, the AAFP calls on the FDA to work with the Centers for Medicare & Medicaid Services to increase opportunities for family physicians and other healthcare clinicians to counsel patients about tobacco cessation. We call on the FDA to clarify the interim final rule titled, "Coverage of Certain Preventive Services Under the *Affordable Care Act*"<sup>3</sup> which implements Section 2713 of the *Public Health Service Act* to include both counseling and pharmacotherapy as described in the 2008 Public Health Services guideline. In its 2015 update regarding tobacco cessation, the U.S. Preventive Services Task Force (USPSTF) reinforces its "A" recommendation for these services, and states:

*"The USPSTF recommends that clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and FDA approved pharmacotherapy for cessation to adults who use tobacco."*<sup>4</sup>

Insurance companies and health plans do not provide uniform coverage of tobacco cessation services across the country because both counseling and pharmacotherapy were not specifically mentioned in previous rules on tobacco cessation treatment. Counseling reinforces pharmacotherapy use in the treatment of tobacco dependence and is an effective method to reduce smoking rates. Its use should be emphasized with OTC NRT to increase access to and reimbursement for counseling services. The FDA could play an important role to that end, including expansion of access to quitline services, pharmacy-based counseling, and improved reimbursement for primary care cessation

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counseling. Manufacturers of OTC NRT should provide access to free telephone cessation counseling similar to pharmaceutical company practices for prescription products like varenicline. The AAFP strongly encourages the FDA to work with other federal agencies through existing collaborations such as the Surgeon General's Interagency Committee on Smoking and Health to discuss these issues.

The AAFP offers the following responses to the questions asked by the FDA in this request for comments:

1. *Might there be ways to improve upon the currently available delivery systems to yield new OTC NRT products that might be more effective? If so, what evidence would be needed to support such changes, and how should they be evaluated?*

Exploring OTC NRT products, like 6-mg dose sizes for "gum" may assist in preventing under-dosing, which can lead to relapse. 2-mg sublingual tablets and the nicotine "mouth spray" approved in Canada may deliver nicotine more quickly and could be beneficial and effective new OTC NRT products for Americans. Evaluating these products through clinical trials with comparison to existing FDA-approved products would be appropriate and expedited approval should be considered as NRT has been used in the United States since 1984. FDA should prioritize expanding funding for novel drug delivery system research into OTC NRT to improve efficacy, decrease side effects and decrease the risk of relapse. This research should also prioritize combination therapy and the effectiveness of the novel drug delivery systems in partnership with counseling as a comprehensive cessation treatment.

2. *Are there additional indications or regimens for OTC NRT products that could be explored? Concepts to consider could include relapse prevention, craving reduction, maintenance, reduce to quit, use of short- and long-acting products in combination, or cessation of non-cigarette tobacco products. What evidence would be needed to support each indication or regimen?*

The FDA should approve Combination OTC NRT therapy, such as using the patch plus a short-acting agent (gum, lozenge, nasal spray). In Combination OTC NRT therapy, a patient uses the passive, long-acting patch combined with a "rescue" OTC NRT to help quell acute craving. Combination OTC NRT therapy has a strong evidence base in peer-reviewed literature, successful clinical trials and systematic reviews analyzing its use and effectiveness. The 2013 Cochrane review notes combination OTC NRT was equal to varenicline in cessation success.<sup>5</sup> It is important to provide notes of caution, however. First, the use of OTC NRT prior to the quit date and smoking reduction provides inconsistent results; this method may not be any more effective than abrupt cessation. Second, it appears that the use of OTC NRT prior to the quit date may be effective with patients who have relapsed after trying abrupt cessation and should not be discouraged. Third, use of OTC NRT after the quit date appears to be at least equivalent to the standard quit process and FDA approval of this alternative should be considered. Fourth, relapse prevention with OTC NRT is not as successful when compared to long-term use of bupropion or varenicline. Fifth, OTC NRT seems to have had little success with non-cigarette tobacco use apart from the use of the lozenge form. Further trials with the lozenge, perhaps in combination with varenicline, should be considered for oral tobacco dependence treatment.

3. *What data would be required to demonstrate health benefits of reduction in consumption of combustible tobacco products?*

Both immediate and long-term data would be required to demonstrate the health benefits of reduced consumption of combustible tobacco products. In the short term, several indicators that could be used to demonstrate the health benefits include measuring blood pressure, nicotine levels, and lung capacity before and after the reduction of consumption of tobacco products during a set observation period. Long-term data could include, but would not be limited to, risk of cancer, stroke, heart disease and chronic obstructive pulmonary disease. It is imperative to control for compensation in smoking; for example, the differences in inhalation and smoking closer to the filter, whether smokers reduced consumption during the entire period of the observation, and whether biomarkers determine reduced exposure to the components of smoke known to cause disease. Ideally, all data collected would have a comparison group of tobacco-users that did not quit or reduce smoking of similar demographics to serve as a control group.

4. *Are there OTC NRT products that could be studied for use in combination that might result in reduced tobacco related health impacts? What evidence would be needed to support the safety and efficacy of these products when used in combination?*

Evidence indicates use of the nicotine patch in combination with the gum and lozenge results in improved efficacy when compared with single-NRT forms. We believe the existing evidence should be sufficient to warrant FDA approval of combination therapy, particularly under the guidance of primary care physicians, family physicians and other appropriately trained clinicians.

5. *Is there other information that could be added to labeling for currently approved or new dosage forms of OTC NRT products that would maximize their ability to be used to support smoking cessation? Please consider the various sections of the Drug Facts labeling, including the Uses, Warnings, and Directions sections.*

The AAFP recommends patients should be advised to talk with their family physician or primary care clinician about combination therapy. In addition, patients should receive information about combination therapy and potential benefits. Finally, patients should understand the use of the nicotine patch in combination with a short acting OTC NRT to quell short term cravings may also be a valid form of treatment.

6. *Generally, the labeling of OTC NRT products contains a dosing schedule based on duration of use, and FDA has recommended the labeling on OTC NRT products be modified to include the following: "If you feel you need to use [the NRT product] for a longer period to keep from smoking, talk to your health care provider." What is the impact of longer term NRT treatment? What is the impact on likelihood of cessation or relapse prevention? What data would support an affirmative recommendation to use approved OTC NRT products for durations that exceed those currently included in the Drug Facts labeling of approved OTC NRT products, or would support a chronic or maintenance drug treatment indication for such products?*

Current data is not robust in the use of OTC NRT in relapse prevention or as long-term therapy. There is limited data, including meta-analysis in the 2008 PHS Guidelines, indicating

extended use of NRT is safe and may be effective among some smokers. We support label changes that reflect this, but acknowledge that further research may be needed.

We appreciate the opportunity to provide these comments. Please contact Robert Bennett, Federal Regulatory Manager, at 202-232-9033 or [rbennett@aafp.org](mailto:rbennett@aafp.org) with any questions or concerns.

Sincerely,

A handwritten signature in black ink, appearing to read 'John Meigs, Jr.', with 'MD' written in smaller letters at the end of the signature.

John Meigs, Jr., MD, FAAFP  
Board Chair

### **About Family Medicine**

Family physicians conduct approximately one in five of the total medical office visits in the United States per year – more than any other specialty. Family physicians provide comprehensive, evidence-based, and cost-effective care dedicated to improving the health of patients, families and communities. Family medicine's cornerstone is an ongoing and personal patient-physician relationship where the family physician serves as the hub of each patient's integrated care team. More Americans depend on family physicians than on any other medical specialty.

### **Works Cited**

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