

**Food and Drug Administration  
Center for Drug Evaluation and Research**

**Final Summary Minutes of the Nonprescription Drugs Advisory Committee Meeting  
September 18, 2019**

Location: FDA White Oak Campus, Building 31 Conference Center, The Great Room (Rm. 1503), 10903 New Hampshire Ave, Silver Spring, Maryland.

Topic: The committee discussed data submitted by GlaxoSmithKline Consumer Healthcare Holdings (US) LLC, to support new drug application (NDA) 208425, for over-the-counter (OTC) marketing of nicotine oral spray (1 milligram (mg) per spray). The proposed OTC use is to reduce withdrawal symptoms, including nicotine craving, associated with quitting smoking. The applicant proposes to label the product for adults 18 years and older. The committee was asked to consider whether data support an acceptable risk/benefit profile for the nonprescription use of nicotine oral spray (1 mg per spray) by OTC consumers.

These summary minutes for the September 18, 2019 Nonprescription Drugs Advisory Committee meeting of the Food and Drug Administration were approved on 10/3/19.

I certify that I attended the September 18, 2019 Nonprescription Drugs Advisory Committee meeting of the Food and Drug Administration and that these minutes accurately reflect what transpired.

\_\_\_\_\_/s/\_\_\_\_\_  
Cindy Chee, PharmD  
Acting Designated Federal Officer, NDAC

\_\_\_\_\_/s/\_\_\_\_\_  
Richard A. Neill, MD  
Chairperson, NDAC

## **Final Summary Minutes of the Nonprescription Drugs Advisory Committee Meeting September 18, 2019**

The Nonprescription Drugs Advisory Committee (NDAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met on September 18, 2019, at the FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and GlaxoSmithKline Consumer Healthcare Holdings (US) LLC. The meeting was called to order by Richard A. Neill, MD (Chairperson). The conflict of interest statement was read into the record by Cindy Chee, PharmD (Acting Designated Federal Officer). There were approximately 140 people in the attendance. There were four Open Public Hearing speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

**Agenda:** The committee discussed data submitted by GlaxoSmithKline Consumer Healthcare Holdings (US) LLC, to support new drug application (NDA) 208425, for over-the-counter (OTC) marketing of nicotine oral spray (1 milligram (mg) per spray). The proposed OTC use is to reduce withdrawal symptoms, including nicotine craving, associated with quitting smoking. The applicant proposes to label the product for adults 18 years and older. The committee was asked to consider whether data support an acceptable risk/benefit profile for the nonprescription use of nicotine oral spray (1 mg per spray) by OTC consumers.

### **Attendance:**

**Nonprescription Drugs Advisory Committee Members Present (Voting):** Lorenzo Di Francesco, MD, FACP, FHM; Neil J. Farber, MD, FACP; Tonya S. King, PhD; Daniel L. Krinsky, MS, RPh; Pamela Mack-Brooks, MSN, RN, NEA-BC (Consumer Representative); Richard A. Neill, MD (Chairperson); Maria C. Pruchnicki, PharmD, FCCP, BCPS, BCACP, CLS; Christianne L. Roumie, MD, MPH

**Nonprescription Drugs Advisory Committee Members Not Present (Voting):** Elma D. Baron, MD; Victor Wu, MD, MPH

**Acting Industry Representative to the Committee (Non-Voting):** Nora Zorich, MD, PhD (Acting Industry Representative)

**Temporary Members (Voting):** Susan J. Curry, PhD; Dorothy Hatsukami, PhD; Suchitra Krishnan-Sarin, PhD; David B. Nelson, MD, MSc, FAAP; Ruth Parker, MD; Abigail B. Shoben, PhD; Jill Thomas, RMP, NMT (Patient Representative)

**FDA Participants (Non-Voting):** Theresa Michele, MD; Jenny Kelty, MD; David Petullo, MS; Celia Winchell, MD

**Acting Designated Federal Officer (Non-Voting):** Cindy Chee, PharmD

**Open Public Hearing Speakers:** Dennis Henigan (Campaign for Tobacco-Free Kids); David Spangler (Consumer Healthcare Products Association); Erika Sward (American Lung Association); Nina Zeldes (*on behalf of Jack Mitchell*; National Center for Health Research)

***The agenda was as follows:***

Call to Order and Introduction of Committee	<b>Richard Neill, MD</b> Chairperson, NDAC
Conflict of Interest Statement	<b>Cindy Chee, PharmD</b> Acting Designated Federal Officer, NDAC
FDA Introductory Remarks	<b>Jenny Kelty, MD</b> Lead Medical Officer Division of Nonprescription Drug Products (DNDP) Office of Drug Evaluation IV (ODE IV) Office of New Drugs (OND), CDER, FDA
<b>APPLICANT PRESENTATIONS</b>	<b>GlaxoSmithKline Consumer Healthcare Holdings (US) LLC</b>
Introduction	<b>Sue James</b> Vice President & Head of Global Regulatory Affairs GSK Consumer Healthcare
Efficacy Review	<b>Mitchell Nides, PhD</b> President Los Angeles Clinical Trials
Real-World Nicotine Replacement Therapy (NRT) Effectiveness	<b>John Hughes, MD</b> Professor, Board Certified Psychiatrist University of Vermont College of Medicine
Safety Review	<b>Rajesh Mishra, MD, PhD</b> Vice President Global Medical & Clinical Sciences Johnson & Johnson Consumer Inc.
Consumer Studies Review	<b>Julie Aker, MT (ASCP)</b> President & CEO Concentrics Research
Benefit-Risk Summary and Conclusion	<b>Sue James</b>
Clarifying Questions	

**BREAK**

**FDA PRESENTATIONS**

Efficacy and Safety Data in Clinical Trials     **Sarah Arnold, MD, MPH**  
Medical Officer  
Division of Anesthesia, Analgesia, and Addiction  
Products  
Office of Drug Evaluation II (ODE II)  
OND, CDER, FDA

**Katherine Meaker, MS**  
Statistical Reviewer  
Division of Biometrics II, Office of Biostatistics Office  
of Translational Sciences, CDER, FDA

Postmarketing Safety Data     **Martha Lenhart, MD, PhD**  
Medical Officer  
DNDP, ODE IV, OND, CDER, FDA

Label Comprehension Study     **Barbara Cohen, MPA**  
Social Science Analyst  
DNDP, ODE IV, OND, CDER, FDA

Clarifying Questions

**LUNCH**

Open Public Hearing

Charge to the Committee     **Theresa Michele, MD**  
Division Director  
DNDP, ODE IV, OND, CDER, FDA

Questions to the Committee/Committee  
Discussion

**BREAK**

Questions to the Committee/Committee  
Discussion

**ADJOURNMENT**

***Questions to the Committee:***

1. **DISCUSSION:** Discuss the efficacy of nicotine mouth spray (1mg per spray) as an over-the-counter (OTC) smoking cessation aid. Consider the differences between the efficacy data from studies A6431111 and NICTDP3038.

***Committee Discussion:*** *The committee members were unclear as to whether Study 38 (a.k.a. Study NICTDP3038) provided clinical significance, possibly due to differences in population,*

*methodology, or ease of use of nicotine mouth spray (NMS) compared to Study 11 (a.k.a. Study A6431111). They commented on the differences between quit-rates with NMS compared to other nicotine replacement therapy (NRT) clinical studies. Some committee members expressed concerns regarding the differences in the two studies, such as psycho-social counseling provided in Study 11, but not in Study 38. Some members noted that smokers wanting to quit would seek out a health professional's help which could increase the efficacy of NMS, while others noted that despite the marginal statistical significance seen in Study 38, it was beneficial for the few patients who successfully quit smoking with NMS. Some committee members noted that Study 11 did show efficacy but does not mimic the OTC setting and was not conducted in the United States. The committee members also commented that they would like to see a head-to-head study comparing NMS to a current NRT therapy already on the market. Please see the transcript for details of the Committee discussion.*

2. **DISCUSSION:** Discuss the results of the label comprehension study and their implications for efficacy in the OTC consumer setting.

***Committee Discussion:** The committee members commented that the results of the label comprehension study showed that consumers have trouble understanding the multi-step usage instructions of NMS. They also noted that the directions are difficult to follow and not adequately communicated, and that consumers will need more guidance. Some committee members commented on the need to add the ability to track the number of sprays used (i.e., spray counter) and a clearer product label. One committee member suggested the inclusion of guidance for patients post 12 weeks NMS usage if the patient was not successful in quitting smoking. The committee members also commented on the small font size of the instructions on the label and expressed concerns that many consumers in the label comprehension study did not open the package flap that included additional usage instructions. Please see the transcript for details of the Committee discussion.*

3. **VOTE:** Do the data provide substantial evidence of efficacy of nicotine mouth spray (1mg per spray) as a smoking cessation aid in the OTC setting?
  - a. If no, what further data should be obtained?

**Vote Result:**      Yes: 8              No: 7              Abstain: 0

***Committee Discussion:** A slight majority of the committee agreed that the data provide substantial evidence of efficacy of NMS as a smoking cessation aid in the OTC setting. The committee members who voted "Yes" commented that NMS provides another modality of NRT for consumers, but NMS needs clearer directions. Some of these members noted that the number needed to treat (NTT) of 40 was relatively high, but NMS will be effective in many due to the number of people who are trying to quit smoking in the United States. The committee members who voted "No" commented on the lack of substantial evidence of efficacy and suggested improvements on product labeling, conducting a blinded non-inferiority trial comparing NMS to other NRT therapies, another trial in the OTC setting in the United States, and a study assessing the consumer's ability in counting of doses and tapering NMS therapy. Please see the transcript for details of the Committee discussion.*

4. **DISCUSSION:** Discuss the safety of nicotine mouth spray (1mg per spray) as a smoking cessation aid in the OTC setting.

*Committee Discussion:* Some committee members stated that safety was well established from the post-marketing and clinical studies provided, and they had no concerns for its safety. Other members expressed concerns regarding concurrent use of vaping products or NRT therapy with NMS. A few members commented on the possible dependence to NMS due to length of use seen in the clinical studies, while others noted that dependence to NMS is not as worrisome as dependence to cigarettes. The committee members also expressed concern for oral mucosal changes found with use of NMS and suggested further investigation. A committee member suggested inclusion of warning on the label for children and pets due to the liquid dosage form and the possibility of ingestion. Please see the transcript for details of the Committee discussion.

5. **DISCUSSION:** Discuss the potential for abuse of nicotine mouth spray (1 mg per spray) by the adult and pediatric populations in the OTC setting. Consider its pharmacokinetic profile and other characteristics that are different from currently marketed OTC nicotine replacement therapy products.

*Committee Discussion:* Most of the committee members expressed concerns with potential abuse in pediatric patients as this population was not studied. One committee member noted that there was no evidence of marketing to children by the Applicant, while another noted that vaping products do not advertise to children either, but still pose a problem in adolescents. Another committee member commented that NMS is not only an additional form of nicotine that could get into the hands of youth, but that use could be more easily hidden, as there is no exhaled smoke or vapor. Many of the committee members were concerned with the ease of online purchase by adolescents. Please see the transcript for details of the Committee discussion.

6. **VOTE:** Do the data provide substantial evidence of safety of OTC use of nicotine mouth spray (1 mg per spray)?
- a. If no, what further data should be obtained?

**Vote Result:**      Yes: 9              No: 6              Abstain: 0

*Committee Discussion:* The majority of the committee members agreed that the data provide substantial evidence of safety of OTC use of NMS. The committee members who voted “Yes” commented on the tolerable safety signal based on the available European post-marketing data and thought that NMS was comparable to other NRTs currently available; however, some expressed concern with possible transfer of addiction from another source of nicotine to NMS. The committee members who voted “No” expressed concerns about abuse potential, misuse by young users, and dependence. One member noted that the available post-marketing surveillance data is insufficient and does not reflect abuse by youths. The committee members also commented on the uncertain regulation amongst young users and

*the appeal of the product to this population, and the need for post-marketing surveillance in the US. Please see the transcript for details of the Committee discussion.*

7. **VOTE:** Is the benefit-risk profile of nicotine mouth spray (1 mg per spray) supportive of OTC use as a smoking cessation aid?
- a. If yes, do you have additional comments or recommendations for labeling?
  - b. If no, what further data should be obtained?

**Vote Result:**            Yes: 9            No: 6            Abstain: 0

**Committee Discussion:** *The majority of the committee members agreed that the benefit-risk profile of NMS is supportive of OTC use as a smoking cessation aid. The committee members who voted “Yes” commented that having more options to quit smoking is more beneficial to patients. Several members expressed that the labeling could be improved and tapering instructions need to be made clearer. One member commented that the product should be modified to be less attractive/appealing and should include the warning (like cigarettes are required to have) that the product contains nicotine, an addictive compound. The committee members who voted “No” commented on the marginal efficacy and the abuse potential among adolescents. One member noted that the quit rate in Study 38 reflects the lack of efficacy of NMS. The committee overall suggested additional efficacy trials in the US and improvements in the instructions on the label. Please see the transcript for details of the Committee discussion.*

The meeting was adjourned at approximately 4:35 p.m.