AMERICAN PSYCHIATRIC ASSOCIATION

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January 12, 2023

Robert M. Califf, M.D.
Commissioner of Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20857

RE: Safety and Effectiveness of Certain Naloxone Hydrochloride Drug Products for Nonprescription Use; Request for Comments (Docket No: FDA-2022-N-2673)

Dear Commissioner Califf,

The American Psychiatric Association (APA) is the nation's medical specialty society that represents more than 37,000 psychiatric physicians and their patients. We appreciate the opportunity to respond to FDA's Request for Comments on the preliminary assessment that certain formulations of naloxone are safe and effective for over the counter (OTC) use.

The number of drug overdose deaths in the United States has been increasing over the last 20 years, with a sharp rise in the last half-decade that has been largely attributed to synthetic opioids (primarily fentanyl). In 2020 alone, the number of drug overdose deaths exceeded 100,000, a 28% increase from the prior year, with three out of four deaths involving opioids. Many of these deaths could have been prevented with naloxone, a rapid-acting opioid antagonist that can be used to reverse an opioid overdose, though numerous legal and financial barriers have prevented the largescale distribution and use of this lifesaving medication.

One such barrier is naloxone's current status as a prescription only medication. This prevents individuals from being able to purchase naloxone, as not everybody is willing or able to visit a physician to receive a prescription. Given the ease of use and low risk profile, APA supports FDA's preliminary assessment that naloxone nasal spray and autoinjector formulations are safe and effective for OTC use. APA encourages FDA to consider several issues highlighted below to avert any potential consequences of a switch from prescription to nonprescription status and potential actions that FDA could consider to address them.

End-user Education

APA supports expanded access to naloxone, along with appropriate training and education, for bystanders, family members, and other individuals who may be in a

position to initiate early response to opioid overdose, including EMTs, paramedics, corrections officers, and law enforcement.[1] If naloxone becomes an OTC product, it is vital that individuals understand how to identify and respond to an overdose, including the actions necessary after administration and reversal. This could be accomplished with a packing insert that clearly describes the signs of an opioid overdose, outlines the steps necessary to administer naloxone, and reminds the user to call emergency services. An additional, we recommend that each package of naloxone include a wallet card with printed use instructions and a QR code that links to an online video on how to manage an opioid overdose.

National Supply

Naloxone is already a product that has faced supply issues. Increasing access to naloxone via OTC purchase may decrease access to high-risk populations via bulk distribution of community-based organizations. **APA encourages FDA to add naloxone nasal spray to the list of FDA Essential Medications, along with IV and IM formulations of naloxone.** This would open federal resources and prioritize investment in long-term domestic manufacturing. Furthermore, FDA should reexamine data regarding expiration dates to ensure that useful inventory has a maximal shelf life and coordinate with industry, distributors, and federal and state authorities to move product to areas of high need prior to expiration.

Cost

Cost barriers must be mitigated through payers' coverage of OTC formulations of naloxone. For example, Medicare does not pay for some forms of nicotine replacement therapy such as the patch, gum, or lozenges due to them being OTC. **APA encourages FDA to work with CMS and other payers to keep cost down for the most vulnerable populations.** Moreover, FDA can prioritize the review of abbreviated new drug applications so that generics of the nasal spray and IM autoinjector are available for purchase at a lower price. Finally, prescribers should also be advised to continue writing naloxone prescriptions for patients at risk, as payers can continue to cover naloxone without OTC packaging, as is the case with fluticasone propionate nasal spray (Flonase) and levonorgestrel.[2]

Thank you for the opportunity to respond to this Request for Comments on the preliminary determination for the safety and effectiveness of intranasal and autoinjector formulations of naloxone as OTC. If you have questions or would like to discuss these comments in more details, please contact Brooke Trainum, Director of Practice Policy, at btrainum@psych.org.

Sincerely,

Saul M. Levin, M.D., M.P.A., FRCP-E, FRCPsych
Chief Executive Officer & Medical Director

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[1] Joint Position Statement of the American Psychiatric Association and The American Academy of Addiction Psychiatry. (December 2015) Opioid Overdose Education and Naloxone Distribution. Located online at: https://psychiatry.org/getattachment/b54f868d-33dc-4a0e-b773-9d001079efb1/Position-Opioid-Overdose-Education-and-Nalaxone-Distribution.pdf.

[2] Walsh, K. L., & Bratberg, J. P. (2021, July 2). Plan N: The Case For Over-The-Counter Naloxone. *Health Affairs*. https://www.healthaffairs.org/do/10.1377/forefront.20210630.42921/