November 24, 2022

DELIVERED ELECTRONICALLY

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Docket No. FDA–2021–N–0862; Nonprescription Drug Product With an Additional Condition for Nonprescription Use

The Naloxone Policy Section of the Justice Roundtable's Harm Reduction Working Group – the undersigned group of policy advocates focused on reducing opioid overdose deaths in the U.S. – appreciates the opportunity to provide comments in response to Federal Register notice FDA-2021-N-0862.

We write to express our support for FDA's intent to establish a pathway for medications to be approved as nonprescription drug products with an "additional condition for nonprescription use" (ACNU). We also write to emphasize the urgent compelling need for easier access to naloxone, which is currently available only by prescription in the U.S. We urge FDA to use this rule, should it be adopted, to increase access to naloxone through the approval of nonprescription naloxone products. The potential use of this pathway for naloxone is a perfect example of how the rule could be used to "improve the public health by broadening the types of nonprescription drug products available to consumers."[1] We further suggest that FDA should, if this rule is adopted, strongly consider moving at least one naloxone product to ACNU status on its own authority, and should modify the rule as applicable to explicitly permit that possibility.[2]

The Opioid Overdose Crisis

Opioid overdose deaths are a public health crisis that has been exacerbated recently by the COVID-19 pandemic[3] and the adulteration of much of the U.S. illicit drug supply with fentanyl.[4] Over 107,000 people died of drug overdose in the U.S. in 2021; nearly 76,000 of these deaths involved an opioid.[5] Many of those 76,000 people would be alive today if they had received naloxone.

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[1] 21 CFR Parts 201 and 314, Vol. 87, No. 123, p. 38131 (check cite form)
[2] FDA clearly has the authority to take this action. *See* Davis CS, Carr D. *Over the counter naloxone needed to save lives in the United States*. Preventive medicine 2020;130:105932; Kaufman, M. *FDA says it can take away drugs' prescription status.* Washington Post, Apr. 26, 2003, FDA Says It Can Take Away Drugs' Prescription Status - The Washington Post.
[3] Centers for Disease Control and Prevention (2020), Overdose Deaths Accelerating During COVID-19 Expanded Prevention Efforts Needed
[4] Centers for Disease Control and Prevention, "Understanding the Epidemic" *citing* Gladden RM, Martinez P, Seth P. Fentanyl law enforcement submissions and increases in synthetic opioid-involved overdose deaths - 27 states, 2013 -2014. MMWR MorbMortal Wkly Rep. 2016; 65:837-43.
[5] National Center for Health Statistics, *Vital Statistics Rapid Release: Provisional Drug Overdose Death Counts,* https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm (Accessed on Oct. 20, 2022).

The Need for Expanded Naloxone Access

As the Administration is well aware, naloxone is safe and effective medication that rapidly reverses opioid overdose.[6] It prevents overdose death and reduces potential disability caused by respiratory depression.[7] It is not a controlled substance and has no misuse potential.[8] Reducing time to naloxone administration is critical, as the risk of irreversible cell death increases with the amount of time the person experiencing overdose is hypoxic.[9] Underscoring its safety, naloxone has been available over the counter in other countries for some time: in Italy since 1996, in Australia since 2016, in Canada since 2016 (nasal only), and in France since 2019.[10]

Unfortunately, naloxone is often not available when and where it is needed. People who use drugs, and their friends and family members, are often the first, and sometimes the only, individuals to respond to an opioid overdose.[11] According to Centers for Disease Control and Prevention data covering eleven states, bystanders were present at approximately 42% of prescription-only, 44% of illicit-only, and 45% of combined opioid-related deaths in 2016 and 2017, but naloxone was administered in only 0.8%, 4.3%, and 4.4% of cases, respectively.[12] The medication's prescription status is a key barrier to layperson access and administration.[13]

People with opioid use disorder often experience difficulties obtaining and filling prescriptions for naloxone, including but not limited to financial barriers and stigma against people who use drugs.[14] Approving naloxone products that do not become available as traditional nonprescription products – on the FDA's own authority, it necessary – as "nonprescription with ANCU" is a timely and logical next step in addressing the opioid overdose epidemic.

To increase access to prescription naloxone , each U.S. state has made legal changes to exempt the drug from many otherwise existing restrictions that apply to prescription medications.[15] While these changes have increased community access to the medication and contributed to decreases in opioid-

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[6] Kerr, D., Kelly, A. M., Dietze, P., Jolley, D., & Barger, B. (2009). Randomized controlled trial comparing the effectiveness and safety of intranasal and intramuscular naloxone for the treatment of suspected heroin overdose. Addiction (Abingdon, England), 104(12), 2067–2074. https://doi.org/10.1111/j.1360-0443.2009.02724.

[7] Gertner, A. K., Domino, M. E., & Davis, C. S. (2018). Do naloxone access laws increase outpatient naloxone prescriptions? Evidence from Medicaid. Drug and alcohol dependence, 190, 37–41.

[8] Davis, C.S., Burris, S., Beletsky, L., Binswanger, I., 2016. Co-prescribing naloxone does not increase liability risk. Subst. Abus. 37, 498–500.

[9] *Ibid.*

[10] European Monitoring Centre for Drugs and Drug Addiction "Take-home Naloxone"; Pricolo A, Nielsen S. Naloxone rescheduling in Australia: Processes, implementation and challenges with supply of naloxone as a 'pharmacist only' over-the-counter medicine. Drug Alcohol Rev. 2018 May;37(4):450-453. doi: 10.1111/dar.12547. Epub 2017 Apr 27. PMID: 28449379.

[11] Bennett, A.S., Bell, A., Doe-Simkins, M., Elliott, L., Pouget, E., Davis, C., 2018. From Peers to Lay Bystanders: Findings from a Decade of Naloxone Distribution in Pittsburgh, PA. Journal of Psychoactive Drugs:1-7.

[12] C. L. Mattson, et al., *Opportunities to Prevent Overdose Deaths Involving Prescription and Illicit Opioids, 11 States, July 2016-June 2017*, 67 MMWR MORB MORTAL WKLY REP 34, 945-51 (2018).

[13] 39. Davis CS, Carr D. Over the counter naloxone needed to save lives in the United States. Preventive Medicine 2020; 130:105932.

[14] Corrigan, P.W., Nieweglowski, K., 2018. Stigma and the public health agenda for the opioid crisis in America. Int J Drug Policy 59:44-49; Green, T.C., Case, P., Fiske, H., Baird, J., Cabral, S., Burstein, D., Schwartz, V., Potter, N., Walley, A.Y., et al., 2017. Perpetuating stigma or reducing risk? Perspectives from naloxone consumers and pharmacists on pharmacy-based naloxone in 2 states. J Am Pharm Assoc (2003) 57:S19-S27 e4.

[15] C. Davis & D. Carr, *State legal innovations to encourage naloxone dispensing*, 57 J AM PHARM ASSOC S181-84 (2017); C. Davis & D. Carr, *Legal changes to increase access to naloxone for opioid overdose reversal in the United States*, 157 DRUG ALCOHOL DEPEND 112 (2015).

related overdose deaths, the fact that naloxone is not immediately present at the scene of many overdoses and the continued increase in opioid-related mortality indicates that they are insufficient and that further regulatory measures are needed.[16]

FDA Action Needed to Save Lives

Despite the filing of several citizen petitions, FDA has failed to modify naloxone's prescription status, and manufacturers have neither requested nor appear likely to request that FDA switch an existing prescription-only product to OTC status. Therefore, it appears that FDA action to utilize the ACNU pathway may be a viable path to remove some of the current barriers to naloxone access. As many individuals have previously noted, federal regulations mandate that that "any drug limited to prescription use... shall be exempted from prescription-dispensing requirements when the [FDA] Commissioner finds such requirements are not necessary for the protection of the public health."[17] This is clearly the case with naloxone.

We note that FDA has recently issued a preliminary assessment that certain types of naloxone products may be approvable as safe and effective for nonprescription use.[18] We agree. We also strongly suggest that FDA use the ACNU pathway to approve naloxone products that it does not find appropriate for traditional OTC labeling, including but not limited to the 0.4mg/mL injectable product widely distributed by syringe services programs and that has safely been used by people who inject drugs to reverse tens of thousands of overdoses.

Conclusion

Naloxone saves lives, but only when it is immediately available at an overdose. We are excited about the additional pathway the proposed rule presents for increasing naloxone access. However, we urge FDA to act on its own authority under this or any mechanism to move naloxone to a nonprescription status. FDA should also encourage and incentivize manufacturers to market naloxone products as OTC or ACNU, or move a product to OTC or ACNU status under its own authority.

If you have any questions about this comment please contact Mary Sylla, JD, MPH, Director of Overdose Prevention Policy & Advocacy, National Harm Reduction Coalition at sylla@harmreduction.org or (510) 216-3524.

Sincerely,

Corey Davis, Director, Harm Reduction Legal Project, Network for Public Health Law
Daliah Heller, Vice President, Drug Use Initiatives, Vital Strategies
Elizabeth Jones, Project Director, Overdose Prevention Initiative
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[16] C. McClellan, et al., *Opioid-overdose laws association with opioid use and overdose mortality*, 86 ADDICT BEHAV (2018); B. H. Lambdin, et al., *Naloxone laws facilitate the establishment of overdose education and naloxone distribution programs in the United States*, 188 DRUG ALCOHOL DEPEND 370 (2018).
[17] 21 C.F.R. § 310.200(b).
[18] Safety and Effectiveness of Certain Naloxone Hydrochloride Drug Products for Nonprescription Use; Request for Comments, 87 Fed. Reg. 68, 702 (Nov. 16, 2022).