

November 4, 2021

Kaléo Inc.
111 Virginia Street
Richmond, VA 23219

Dear Stakeholder:

On behalf of the physician and medical student members of the American Medical Association (AMA), I write to request that you submit the appropriate applications to the U.S. Food and Drug Administration (FDA) to make naloxone available as a nonprescription over the counter (OTC) medication. The nation's drug-related overdose and death epidemic is being fueled by increasing levels of illicit fentanyl, fentanyl analogs, and drugs contaminated with illicit fentanyl. Naloxone has proven its efficacy in saving lives from opioid-related overdose. Without this medication, it is likely that tens of thousands more Americans would be dead from an opioid-related overdose. **At this stage in the nation's drug overdose epidemic, there is no valid clinical, public policy, or ethical reason for drug manufacturers to delay OTC applications.**

AMA policy expressly calls on manufacturers to submit OTC applications. Manufacturers of overdose reversal agents can take a drug that has already been approved for prescription use by the FDA and make it available OTC.¹ The FDA has expressly supported making naloxone a nonprescription OTC product, encouraging drug companies to enter the OTC market by granting priority review to all generic applications for drugs that can be used as emergency treatment of known or suspected opioid overdose.²

The FDA has also created two model labels for both versions of the drug – one for the nasal spray and one for the auto-injector.³ In an unprecedented step, the FDA has already designed, tested, and validated these key labeling requirements necessary to approve an OTC version of naloxone.⁴ The FDA has even developed a model Drug Facts label with pictogram instructions to ensure anyone with access can effectively administer it.⁵ This was the first time the FDA proactively developed and tested a drug label to support OTC development. Any application for an OTC version of naloxone that a manufacturer must complete, therefore, will be easier than most OTC applications since FDA has already completed and approved the labeling portion.

¹ P'SHIP END ADDICTION, *FDA Takes Step to Allow Drugs Companies to Sell Naloxone Without Prescription*, (Jan. 2019), <https://drugfree.org/drug-and-alcohol-news/fda-takes-step-to-allow-drug-companies-to-sell-naloxone-without-prescription/>.

² *Supra* note 6.

³ *Supra* note 9.

⁴ FOOD & DRUG ADMIN., *Statement from FDA Commissioner Scott Gottlieb, M.D. on Unprecedented New Efforts to Support Development of Over-The-Counter Naloxone to Help Reduce Opioid Overdose Deaths* (Jan. 17, 2019), <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-unprecedented-new-efforts-support-development-over>.

⁵ *Supra* note 6.

Changing the status of all naloxone products to nonprescription and thereby making them available OTC will strengthen the defensive strategies against the nation's drug overdose epidemic by reducing consumer apprehension. It will also ensure that this opioid-related overdose reversal agent is more widely available.

Last year an unprecedented 93,000 people died in the United States from drug-related overdoses, a rise of nearly 30 percent from 2019.⁶ Since 1999, drug-related overdoses have claimed the lives of more than 900,000 people.⁷ The stress and anxiety produced by the COVID-19 pandemic led to increased substance use.⁸ Coupled with disrupted access to outreach and treatment facilities and increased social isolation, this upsurge of substance use undoubtedly contributed to the increase in overdose deaths.⁹ If trends continue at the current pace, drug overdose deaths will surpass the total number of casualties across all major U.S. wars by 2021.¹⁰

Naloxone has decades of evidence demonstrating that it saves lives. There are three FDA-approved forms of naloxone – injectable, auto-injector, and nasal spray. All three forms currently require a prescription, a condition that limits access for those who are apprehensive to disclose substance abuse issues and for those individuals without health insurance who cannot afford the cost of the product.¹¹

States have increased access by adopting pharmacy-based prescription models to increase availability, including a variety of laws that allow prescribers to prescribe naloxone to patients at risk for overdose.¹² Most states permit pharmacies to dispense naloxone under a standing order, which takes the place of an individual prescription from a provider.¹³ In addition to these measures, some states have permission for “third-party prescriptions” that authorize doctors and pharmacists to prescribe and dispense naloxone to someone who is not directly at risk for an overdose.¹⁴ **While these actions have laudably tried to expand the availability of naloxone, naloxone remains largely unreachable to those most at risk of overdose.**¹⁵ Our nation needs more readily available, evidence-based tools at its fingertips to save lives from overdose.

The AMA and our physician and student members support and encourage individuals to purchase naloxone without the fear of the “drug addict” stigma associated with the overdose reversal treatment.

⁶ Ahmad FB et al., *Provisional Drug Overdose Death Counts*, NAT'L. CTR. HEALTH STAT. (2021), <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>.

⁷ *Wide-Ranging Online Data for Epidemiologic Research (WONDER)*, NAT'L CTR. HEALTH STAT., <https://wonder.cdc.gov/> (last updated July 22, 2021).

⁸ Ahmad, *supra* note 1.

⁹ Sara Glick et al., *The Impact of COVID-19 on Syringe Services Programs in the United States*, 24 AIDS BEHAV. 2466, 2466–2468 (Apr. 24, 2019), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7182093/>.

¹⁰ *The Rise of Drug Deaths in America*, AM. ADDICTION CTR. (Feb. 23, 2021), <https://drugabuse.com/featured/the-rise-of-drug-deaths-in-america/>.

¹¹ FOOD & DRUG ADMIN., *Press Release, Statement on Continued Efforts to Increase Availability of All Forms of Naloxone to Help Reduce Opioid Overdose Deaths* (Sept. 20, 2019), <https://www.fda.gov/news-events/press-announcements/statement-continued-efforts-increase-availability-all-forms-naloxone-help-reduce-opioid-overdose>.

¹² Elizabeth Donovan et al., *Beliefs Associated with Pharmacy-Based Naloxone: a Qualitative Study of Pharmacy-Based Naloxone Purchasers and People at Risk for Opioid Overdose*, 96 J. URB. HEALTH 367, 367-378 (June 2019), [ncbi.nlm.nih.gov/pmc/articles/PMC6565759/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6565759/).

¹³ *Id.*

¹⁴ EDU. DEVELOPMENT CTR., *State Naloxone Access Laws*, <https://preventionsolutions.edc.org/services/resources/state-naloxone-access-laws> (last visited July 27, 2021); see also NAT'L. ALL. MODEL STATE DRUG LAWS, *Naloxone Access: Status of State Laws Map (2015)*, <https://namsdl.org/wp-content/uploads/Naloxone-Access-Status-of-State-Laws-Maps.pdf>.

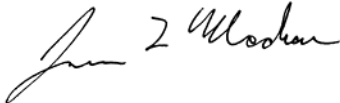
¹⁵ Kendra Walsh & Jeffrey Brathberg, *Plan N: The Case For Over-The-Counter Naloxone*, Health Affairs Blog (July 2, 2021), <https://www.healthaffairs.org/doi/10.1377/hblog20210630.42921>.

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The AMA believes that making all naloxone products available OTC and ensuring the privacy of consumers will reduce the number of deaths from opioid-related overdoses. Lives are on the line, and we strongly request your support to engage in these positive efforts to save them by submitting applications to the FDA for OTC naloxone.

Thank you for your consideration. If you have any questions, please contact Daniel Blaney-Koen, JD, Senior Legislative Attorney, AMA Advocacy Resource Center at daniel.blaney-koen@ama-assn.org.

Sincerely,

A handwritten signature in black ink, appearing to read "Jim L Madara". The signature is written in a cursive, flowing style.

James L. Madara, MD