January 17, 2023

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

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

Submitted via www.regulations.gov for Docket No. FDA-2022-N-2673

Dear Ayako:

The American Pharmacists Association (APhA) is pleased to submit comments on FDA's Request for Comments titled "Safety and Effectiveness of Certain Naloxone Hydrochloride Drug Products for Nonprescription Use; Request for Comments."

APhA is the only organization advancing the entire pharmacy profession. APhA represents pharmacists, student pharmacists, and pharmacy technicians in all practice settings, including but not limited to community pharmacies, hospitals, long-term care facilities, specialty pharmacies, community health centers, physician offices, ambulatory clinics, managed care organizations, hospice settings, and government facilities. Our members strive to improve medication use, advance patient care, and enhance public health.

As FDA considers additional approaches to facilitate access to naloxone, we respectfully request FDA considers the potential unintended consequences of a switch from prescription to nonprescription status for certain naloxone products, and actions FDA could consider to address them, including but not limited to, impacts on community-based naloxone distribution programs and consumers, drug shortages, and the distribution and supply of naloxone.

APhA's House of Delegates passed policy in 2021 related to naloxone availability. The policy states:

> **Increasing Access to and Affordability of Naloxone (2021)**
> 1. APhA supports policies and practices that increase the availability of naloxone.
> 2. APhA supports the availability of naloxone as both a prescription and non-prescription medication.

3. APhA encourages pharmacists and payers to ensure equitable access to and affordability of at least one naloxone formulation regardless of prescription status.
4. APhA encourages payers to provide fair reimbursement to dispensers of naloxone.

APhA appreciates FDA's efforts to allow greater access to prescription and nonprescription medications, like naloxone, to prevent the significant number of unnecessary deaths from opioid-involved drug overdoses. APhA also encourages FDA to improve access to naloxone by leveraging the expertise of the pharmacist. However, FDA's proposal that certain naloxone products, "have the potential…for use as directed in nonprescription drug labeling without the supervision of healthcare provider," creates a number of unintended consequences (patient safety, regulatory, liability, supply and access concerns). Accordingly, APhA urges FDA meet with stakeholders to address these concerns prior to any status changes to these naloxone products.

Unintended Consequences to Consider for Nonprescription Only Availability of Certain Naloxone Products

Patient Safety and Regulatory Concerns

As FDA states, "[a]s of 2020, all 50 states and the District of Columbia have some form of [naloxone access law] NAL….and [t]hese laws are intended to increase naloxone availability for use in individuals experiencing an opioid overdose." The National Alliance of State Pharmacy Associations (NASPA) has a map, updated as of March 2022, of the varying authorities in states to dispense naloxone through either a statewide protocol or prescriptive authority; statewide standing order; or dispensing without a prescription. FDA also states in the Notice, "[w]e are also aware that some State NALs require pharmacists to provide patient counseling before dispensing naloxone, which may include further information on naloxone safety, risks of opioid overdose, and resources on substance use disorder. We do not know to what extent these factors contribute to the safe and effective use of naloxone without the intervention of a learned intermediary." Making certain naloxone product available only nonprescription would eliminate the patient safety and efficacy impact that these existing state laws and policies provide if patients or caregivers are not properly trained or counseled on how to use these products. States may also respond with additional nonprescription regulatory requirements for these over-the-counter (OTC) sales, which could further impact patient access.

A number of states have also enacted naloxone co-prescribing laws, where naloxone is required to be co-prescribed with certain opioid prescriptions (e.g. prescriptions for opioids prescribed concurrently with prescriptions for benzodiazepines, etc.)., and it is unclear how the availability of nonprescription naloxone would impact naloxone co-prescribing practices. If a patient brings presents a prescription for co-prescribed naloxone and they must purchase it OTC if a

prescription product is not available, they may not buy the naloxone if it is not covered by insurance.

Simultaneous Marketing of Prescription and Nonprescription Naloxone

Supply Concerns

FDA "has interpreted the language in section 503(b)(4) of the FD&C Act to allow simultaneous marketing of drug products with the same active ingredient as prescription in one case and nonprescription in another only if some clinically meaningful difference, such as a difference in indication, strength, route of administration, dosage form, or patient population, exists between the drug products that makes the prescription product safe and effective only under the supervision of a healthcare practitioner licensed by law to administer the drug. Absent a clinically meaningful difference between the products, simultaneous marketing of two drug products with the same active ingredient as, respectively, a prescription and a nonprescription drug product would result in one of the two products being misbranded." In short, "[i]f FDA makes a determination that naloxone products described in this notice are safe and effective for use without a prescription, such products would be misbranded if they bear labeling with the "Rx only" symbol."

As mentioned above, APhA's House of Delegates policy supports the availability of naloxone **as both** a prescription and non-prescription medication.[1]" There are FDA-approved medications that are marketed as both prescription and nonprescription. Some examples of those products include meclizine (Rx: vertigo; OTC: nausea with motion sickness), oxybutynin (Rx: overactive bladder; OTC: overactive bladder in women only), and orlistat (Rx: 120mg for obesity mgt; OTC: 60mg for weight loss). In some cases, the prescription dose is the same as the non-prescription product, and in other cases there are differences in intended uses or packaging. APhA recommends FDA consider a regulatory pathway that would allow simultaneous marketing of prescription and nonprescription naloxone products and determine a "meaningful difference" in product labeling, packaging, or other element to warrant simultaneous marketing.

APhA agrees with FDA that if naloxone manufacturers opt not to switch their prescription naloxone products to nonprescription status after there are nonprescription versions of the same product approved this may impact the supply and availability of these products. Accordingly, FDA should thoroughly examine how this policy change will impact manufacturing capacity and potentially contribute to drug shortages that may not sufficiently meet patient demand before approving nonprescription naloxone.

[1] APhA House of Delegates 2022 Policy Manual
https://www.pharmacist.com/DNNGlobalStorageRedirector.ashx?egsfid=XbMYZdOuE1E%3d

Coverage and Patient Access Concerns

Moving these versions of naloxone from a prescription version to an OTC version would also affect insurance coverage of this critical, life-saving drug. If nonprescription naloxone is approved, private and public payers and their affiliated pharmacy benefit managers (PBMs) may not cover these products, which will only increase patients' out-of-pocket costs and further reduce access. Recent reports have also examined additional patient access concerns with FDA's current approach.

Conclusion

APhA appreciates the opportunity to respond to FDA's request for comments on the safety and effectiveness of certain naloxone hydrochloride drug products for nonprescription use. APhA requests FDA consider the unintended consequences, outlined above, before moving these products OTC and urges FDA to work on solutions that leverage our nation's pharmacists. If you have any questions, please contact Heather Boyd, Director, Health Policy at hboyd@aphanet.org.

Sincerely,

Michael Baxter

Michael Baxter
Acting Head of Government Affairs
American Pharmacists Association