REAGAN-UDALL

FOUNDATION

for the Food and Drug Administration

SUMMARY REPORT

NALOXONE ECONOMIC VIEW

MARCH 2023

Naloxone Economic View

SUMMARY REPORT

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ONE | INTRODUCTION

The Reagan-Udall Foundation for the FDA (FDA Foundation), in collaboration with the U.S. Food and Drug Administration (FDA), conducted a research project to explore the current distribution of naloxone in the U.S. and the potential economic impacts of a change in the prescription-only status of naloxone.

Drug overdose deaths in the U.S. top 100,000 annually.[1] The U.S. Centers for Disease Control and Prevention (CDC) recommend additional policy measures to address this issue, including expanding distribution and use of naloxone,[2] and overdose prevention education. The White House recently proposed a state model law facilitating expanded naloxone access, which includes required health insurance coverage.[3] Given the public health importance of naloxone, many jurisdictions have implemented policies to increase its availability.

In 2018, FDA hosted a meeting to solicit input and advice on strategies to increase naloxone availability.[4] Some experts have suggested transitioning naloxone from prescription to nonprescription status as one option to decrease disparities in access. Also, former FDA Commissioners have spoken about the importance of increasing the availability of naloxone and efforts to encourage the development of an nonprescription product.[5,6]

The transition of prescription products to nonprescription is assumed to yield an economic benefit to both the consumer and the health care system, as well as increase overall sales of a product,[7,8] One concern, however, is that a typical health insurance plan prescription drug benefit, whether public or private, may not include coverage of nonprescription products, thus increasing out-of-pocket (OOP) cost to the consumer if the nonprescription price is greater than a drug benefit copay.

1 Ahmad FB, Cisewski JA, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2023. Designed by LM Rossen, A Lipphardt, FB Ahmad, JM Keralis, and Y Chong: National Center for Health Statistics. https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

2 An opioid antagonist that can reverse opioid overdose.

3 White House releases State Model Law to help make access to naloxone consistent across the country. The White House. https://www.whitehouse.gov/ondcp/briefing-room/2021/11/17/white-house-releases-state-model-law-to-help-make-access-to-naloxone-consistent-across-the-country/. Published July 15, 2022. Accessed December 26, 2022.

4 Office of the Commissioner. FDA Briefing Document. Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee. December 17-18, 2018. https://www.fda.gov/media/121182/download. Accessed December 26, 2022.

5 Office of the Commissioner. 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. U.S. Food and Drug Administration. https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-unprecedented-new-efforts-support-development-over. Accessed December 26, 2022.

6 Office of the Commissioner. Statement on continued efforts to increase availability of all forms of naloxone to help reduce opioid overdose deaths. U.S. Food and Drug Administration. https://www.fda.gov/news-events/press-announcements/statement-continued-efforts-increase-availability-all-forms-naloxone-help-reduce-opioid-overdose. Accessed December 26, 2022.

7 Using the Medicare Advantage Over-the-Counter (OTC) Medicines Program as a Consumer Engagement Tool. Consumer Healthcare Products Association. https://www.chpa.org/about-consumer-healthcare/research-data/research-reports/using-medicare-advantage-over-counter-otc-consumer-engagement. Accessed December 26, 2022.

8 Murphy SM, Morgan JR, Jeng PJ, Schackman BR. Will converting naloxone to over‐the‐counter status increase pharmacy sales? Health Services Research. 2019;54(4):764-772. doi:10.1111/1475-6773.13125

The distribution and payor mix for naloxone differs from the traditional prescription-only product. As a result of a mix of standing orders and provision through community-based organizations, the economic implications of a switch to nonprescription status are less obvious from a consumer perspective. While the OOP cost for consumers is often zero for naloxone – either due to a zero-copay structure from their insurance or because the product is provided free of charge by community-based organizations – the posture of these same providers may change with a switch to nonprescription status.

To explore potential impacts of a nonprescription formulation of naloxone becoming available, particularly on payor decision-making and consumer access and OOP costs, the FDA Foundation performed the following analyses:

1. Describe the current distribution and funding mix for naloxone access, yielding the proportion of naloxone costs supported by commercial insurance, by Medicaid programs, by Medicare/Medicare Advantage, by state and federal funding, and directly by patients.
2. Describe the policy of those payors related to general coverage of nonprescription products, including description of payors that cover nonprescription products. For the patient/consumer payment, describe the availability/applicability of flexible spending accounts and health spending accounts.
3. Explore potential impacts of policy changes to expand coverage for nonprescription products, such as naloxone, in a closed-door payor roundtable.

Background

Opioid Overdose

Opioid overdose persists as a major public health issue in the United States, with rates increasing substantially since 2013 (*Figure 1: Three Waves of Opioid Overdose Deaths*).[9] Fatal opioid overdoses increased by 13% from 2020 to 2021, largely driven by increases in deaths due to fentanyl and its analogs (*Table 1*).[9,10] Every day, 187 people die from an opioid overdose, 24% of which involve a prescription medication.[11]

9 Centers for Disease Control and Prevention. Understanding the Opioid Overdose Epidemic. US Department of Health and Human Services. https://www.cdc.gov/opioids/basics/epidemic.html. Accessed February 6, 2023.

10 U.S. overdose deaths in 2021 increased half as much as in 2020 - but are still up 15%. Centers for Disease Control and Prevention. https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/202205.htm#:~:text=The%20new%20data%20show%20overdose,in%202021%20compared%20to%202020. Published May 11, 2022. Accessed December 26, 2022.

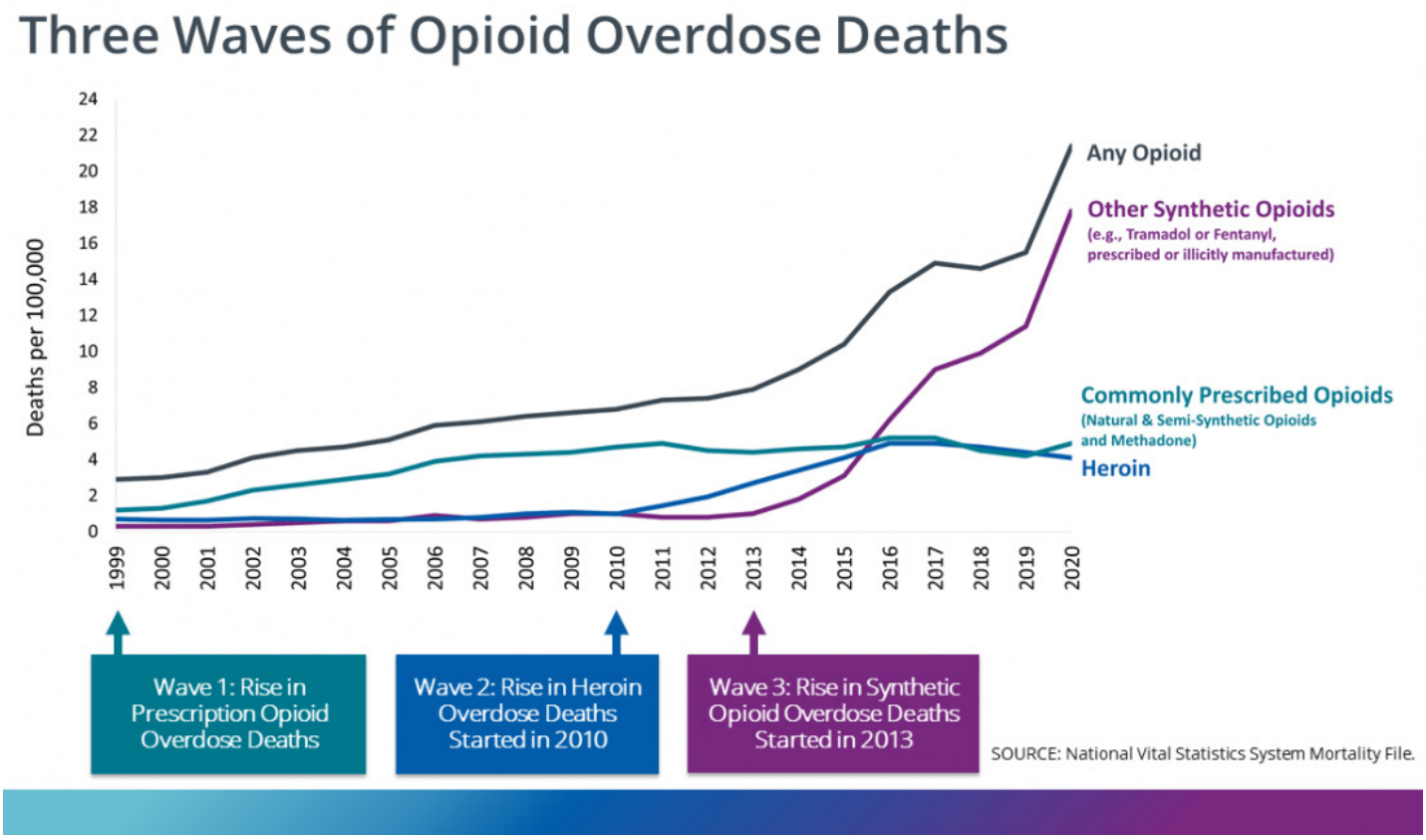
11 Ibid

12 Overdose graphics. Centers for Disease Control and Prevention. https://www.cdc.gov/drugoverdose/resources/graphics/overdose.html. Published June 2, 2022. Accessed December 26, 2022.

Opioid overdoses increased during the COVID-19 pandemic, and disproportionately so for Black Americans and residents of poor, urban areas.[12,13] Despite the increase in opioid overdoses during this time, the number of naloxone prescriptions dispensed per week declined and remained low.[14]

Risk factors for overdose include: changes in tolerance after a period of low- or non-use, changes in drug supply, mixing opioids with respiratory depressants (*benzodiazepines, alcohol, sedatives*) or stimulants (*cocaine, methamphetamine*), chronic health conditions (*asthma, chronic obstructive pulmonary disease, mental health conditions, substance use disorders*), higher doses of prescribed opioids (≥ *100 morphine milligram equivalents*), and a history of past overdose(s).[15]

Figure 1: Three Waves of Opioid Overdose Deaths



13 Ghose R, Forati AM, Mantsch JR. Impact of the COVID-19 pandemic on opioid overdose deaths: A spatiotemporal analysis. Journal of Urban Health. 2022;99(2):316-327. doi:10.1007/s11524-022-00610-0

14 Khatri UG, Pizzicato LN, Viner K, et al. Racial/ethnic disparities in unintentional fatal and nonfatal emergency medical services–attended opioid overdoses during the COVID-19 pandemic in Philadelphia. JAMA Network Open. 2021;4(1). doi:10.1001/jamanetworkopen.2020.34878

15 O'Donoghue AL, Biswas N, Dechen T, et al. Trends in filled naloxone prescriptions before and during the COVID-19 pandemic in the United States. JAMA Health Forum. 2021;2(5). doi:10.1001/jamahealthforum.2021.0393

Table 1: U.S. Overdose Deaths by Drug Type

Drug Type	Deaths (2020)	Deaths (2021)
Synthetic opioids (e.g., fentanyl)	**57,834**	**71,238**
Psychostimulants (e.g., methamphetamine)	**24,576**	**32,856**
Cocaine	**19,927**	**24,538**
Natural/semi-synthetic opioids (prescription)	**13,722**	**13,503**

Preventing Overdose Fatalities: Naloxone

Naloxone saves lives. The National Institute on Drug Abuse (NIDA) Director Dr. Nora Volkow has stated, *"We don't need to keep asking if these things work. Instead, we must find ways to help providers, people, and communities overcome the barriers to implementing these valuable interventions."* [16]

Naloxone prevents death from overdose by blocking the effect of opioids in the body. Naloxone only works to counteract the effects of opioid drugs,[18] but has no effect in reversing the effects of other substances such as alcohol, benzodiazepines, or stimulants. The reversal effects of naloxone are temporary – restoring breathing within 2-3 minutes with effects lasting 30-90 minutes. More than one dose of naloxone may be necessary to prevent death from an overdose depending on the amount of opioid ingested.[18] In addition, naloxone is not harmful if administered in the setting of a non-opioid drug overdose.[19] Naloxone is administered as a nasal spray or as an intramuscular, subcutaneous, or intravenous injection. Naloxone products and administration information are listed in Table 2.

Table 2: Naloxone Products [20]

	Injectable	Intranasal
Brand Availability	Yes (Zimhi™)	Yes (Narcan®, Kloxxado®)
Generic Availability	Yes	Yes
Administration	The proper dose must be drawn up from a vial, or it is provided in prefilled syringes. Usually, it is injected with a needle into muscle, although it also may be administered into a vein or under the skin. Zimhi™ is a prefilled syringe that can be injected into the muscle or under the skin.	These devices contain a prefilled dose that is sprayed into one nostril while the person experiencing an overdose lays on their back.

16 Volkow N. Five areas where "more research" isn't needed to curb the overdose crisis. National Institutes of Health. https://nida.nih.gov/about-nida/noras-blog/2022/08/five-areas-where-more-research-isnt-needed-to-curb-overdose-crisis. Published August 31, 2022. Accessed December 26, 2022.

17 Opioid drugs include: codeine, morphine, oxycodone, hydrocodone, oxymorphone, hydromorphone, methadone, tramadol, fentanyl, buprenorphine, heroin.

18 5 things to know about naloxone. Centers for Disease Control and Prevention. https://www.cdc.gov/drugoverdose/featured-topics/naloxone.html#print. Published October 25, 2022. Accessed December 26, 2022.

19 Wermeling DP. Review of naloxone safety for opioid overdose: practical considerations for new technology and expanded public access. Therapeutic Advances in Drug Safety. 2015;6(1):20-31. doi:10.1177/2042098614564776

20 Naloxone DrugFacts. National Institutes of Health, U.S. Department of Health and Human Services. Updated January 2022. Accessed February 13, 2023. https://nida.nih.gov/publications/drugfacts/naloxone.

Naloxone Access

Barriers and facilitators to naloxone access are listed in Table 3. Opioid reversal agents are only useful if present and administered at the scene of an overdose. Potential bystanders were present but unable to provide life-saving measures such as naloxone in approximately **46%** of fatal overdoses in 2021,[21] and the CDC estimates that naloxone coprescribing occurs as infrequently as once per 69 high-dose opioid prescriptions;[23] both are examples of missed opportunities for intervention.

> *All over the country, putting naloxone in the hands of first responders has saved countless lives. And because it is such a safe drug, it can be put directly in the hands of people who use opioids, their loved ones and friends, and anybody else who may find themselves in a position to save the life of someone overdosing on an opioid. Yet despite the safety and lifesaving value of this drug, there are impediments to widespread use. Naloxone is not available over the counter, which could ease access. Doctors don't always prescribe it to patients who need it, pharmacies don't always stock it, the price may be prohibitive when they do stock it. While many states now have standing orders allowing anyone to get it from the pharmacist without a prescription, people often do not know that. People who offer harm reduction in communities are also affected by costs and product shortages.*[24]
>
> **- NIDA Director Dr. Nora Volkow**

21 Centers for Disease Control and Prevention. State Unintentional Drug Overdose Reporting System (SUDORS). Atlanta, GA: US Department of Health and Human Services, CDC; [2022, December, 26]. Access at: https://www.cdc.gov/drugoverdose/fatal/dashboard

22 Guy GP Jr, Haegerich TM, Evans ME, Losby JL, Young R, Jones CM. Vital signs: pharmacy-based naloxone dispensing—United States, 2012-2018. MMWR Morb Mortal Wkly Rep. 2019;68(31):679-686. doi:10.15585/mmwr.mm6831e1

23 Volkow N. Five areas where "more research" isn't needed to curb the overdose crisis. National Institutes of Health. https://nida.nih.gov/about-nida/noras-blog/2022/08/five-areas-where-more-research-isnt-needed-to-curb-overdose-crisis. Published August 31, 2022. Accessed December 26, 2022.

Table 3: Naloxone Access Barriers and Facilitators [I,II,III,IV,V,VI,VII,VIII,IX,X,XII,XIII,XIV,XV]

Barriers	Facilitators
▸ Prescription-only status ▸ Insurance coverage – copay or coinsurance, prior authorization (PA) requirements ▸ Insurance prescription fill limits (e.g., may only fill the prescription twice in 30 days) ▸ Physical locations of the product – limited to pharmacies (medication/ pharmacy deserts), more limited access in nonurban or rural vs. urban areas ▸ Cost – 20% of adults with opioid use disorder (OUD) are uninsured ▸ Drug shortages ▸ Bias and stigma (requesting the drug from a health care professional or carrying the drug implies illicit drug use) ▸ Structural racism	▸ Nonprescription status ▸ Statewide standing orders or pharmacist prescriptive authority for providing naloxone (no patient-specific prescription) ▸ Co-prescribing of naloxone with an opioid ▸ Affordable or free naloxone ▸ Legislation requiring coverage by insurance without fill limits or PA requirements ▸ Community distribution – harm reduction, schools, libraries, prisons, vending machines ▸ Prescriber, dispenser, and layperson liability immunity ▸ FDA supply chain regulations for harm reduction organizations (see guidance) – can also be a barrier ▸ Prohibition on life insurance companies taking adverse actions against people who have obtained naloxone

Nonprescription Naloxone

A potential shift in prescription-only to nonprescription status for medications requires consideration on the part of sponsors/manufacturers, regulators, payors, health professionals, and consumers. Naloxone is not currently available as a nonprescription medication. Nonprescription drugs meet the following criteria:[24]

- The drug has a high safety margin.
- The drug can be used appropriately by consumers for self-diagnosed conditions.
- The health practitioner is not required for safe and effective use.
- The drug has a low potential for misuse and abuse.
- The product can be adequately labeled to allow safe and effective use without additional instruction.

24 U.S. Food and Drug Administration. Center for Drug Evaluation and Research. Drug applications for nonprescription drugs: NDA and ANDA. U.S. Food and Drug Administration. https://www.fda.gov/drugs/types-applications/drug-application-process-nonprescription-drugs. Accessed February 1, 2023.

25 Robeznieks A. Removing naloxone's RX status is an essential step to save lives. American Medical Association. https://www.ama-assn.org/delivering-care/overdose-epidemic/removing-naloxone-s-rx-status-essential-step-save-lives. Published March 11, 2022. Accessed December 26, 2022.

Numerous professional organizations have called for over-the-counter (OTC) naloxone as a step to improve accessibility.[26,27,28,29,30,31] They recommend removal of prescription status for all formulations or nonprescription status of at least one formulation, regardless of manufacturer requests.

The FDA has taken steps to support availability of nonprescription naloxone on the market, and at the time of this report two manufacturers [32,33] have submitted applications to the FDA for a nonprescription naloxone nasal spray. In addition, the FDA conducted a naloxone OTC label comprehension study to determine whether consumers understood key statements on the label, which was a major step toward safe and effective use of naloxone in the OTC setting.[35]

TWO | NALOXONE DISTRIBUTION

Distribution Data

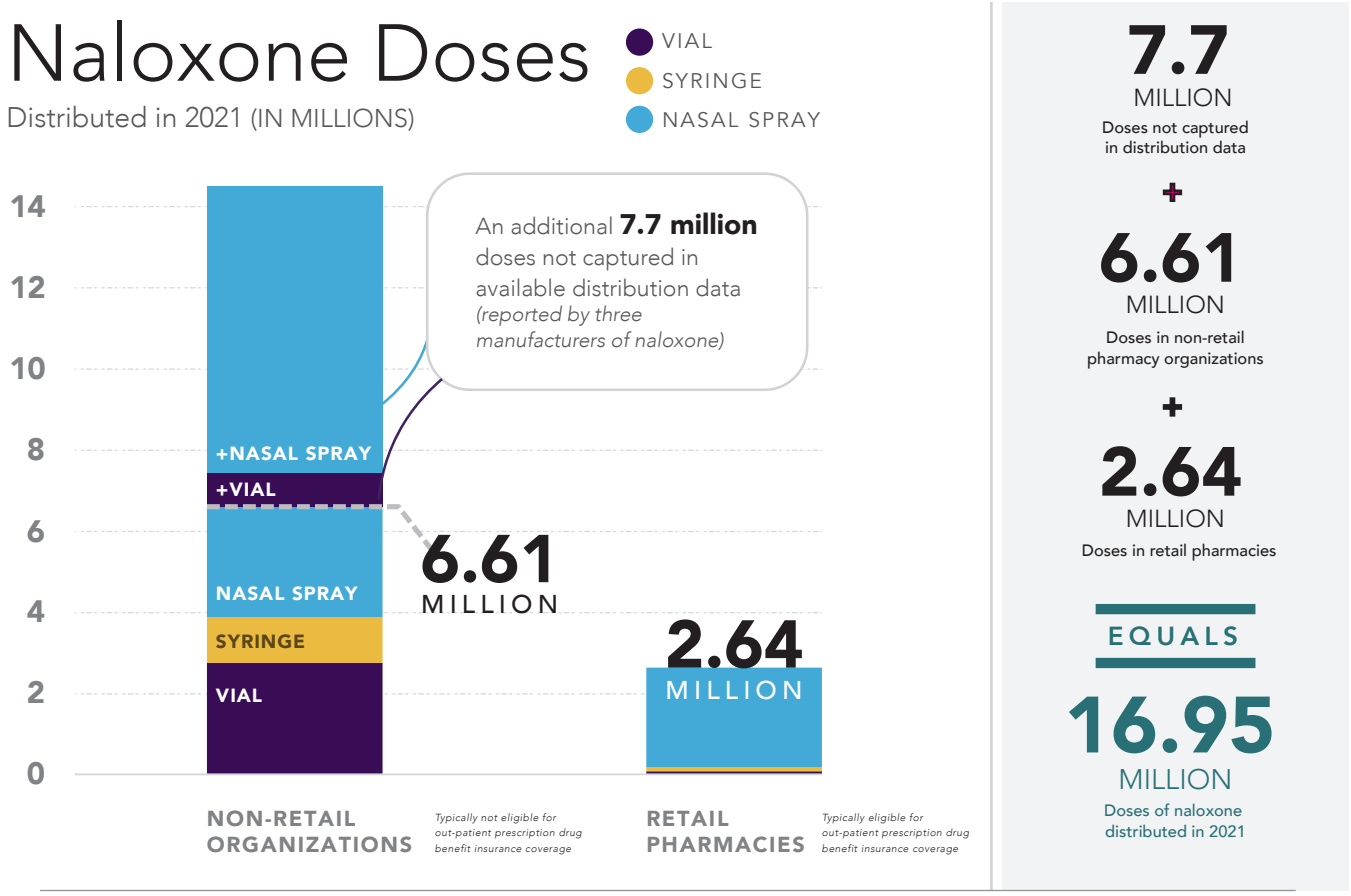
In 2022, we sought to estimate how many doses[37] of naloxone are distributed in the United States annually and what proportion of doses are distributed through pharmacies versus other avenues. We engaged with experts in the field to understand unique distribution considerations for naloxone, including representatives from manufacturing, trade organizations, and academia. A convenience sample of three major manufacturers provided the number of naloxone units distributed in calendar year 2021. These data were cross-referenced with IQVIA National Sales Perspectives (NSP) data queried for January 2021-December 2021 (extracted July 2022 and verified December 2022).[36] To prevent double counting, we did not include doses reported by

26 APhA Policy Manual: American Pharmacists Association. Home. https://aphanet.pharmacist.com/policy-manual?key=naloxone&op=Search. Accessed December 26, 2022.
27 Skelton JB, Dharbhamalla V. The role of Managed Care Pharmacy in coprescribing naloxone for patients with specific risk: Recommendations from the AMCP Addiction Advisory Group. Journal of Managed Care & Specialty Pharmacy. 2022;28(1):100-106. doi:10.18553/jmcp.2022.28.1.100
28 Jawa R, Murray S, Tori M, Bratberg J, Walley A. Federal policymakers should urgently and greatly expand naloxone access. American Journal of Public Health. 2022;112(4):558-561. doi:10.2105/ajph.2021.306699
29 ASAM (American Society of Addiction Medicine). Use of naloxone for the prevention of opioid overdose deaths. Public Policy Statement on the Use of Naloxone for the Prevention of Deaths Background Opioid Overdose Deaths. Retrieved December 26, 2022, from https://www.asam.org/docs/default-source/public-policy-statements/use-of-naloxone-for-the-prevention-of-opioid-overdose-deaths-final.pdf
30 Davis CS, Carr D. Over the counter naloxone needed to save lives in the United States. Preventive Medicine. 2020;130:105932. doi:10.1016/j.ypmed.2019.105932
31 Safety and Effectiveness of Certain Naloxone Hydrochloride Drug Products for Nonprescription Use; Request for Comments. 87 FR 68702 (November 16, 2022). https://www.federalregister.gov/d/2022-24874. Accessed December 26, 2022.
32 Emergent Biosolutions NDA for OTC Narcan® (naloxone HCl) nasal spray Investors.emergentbiosolutions.com. https://investors.emergentbiosolutions.com/news-releases/news-release-details/emergent-biosolutions-announces-us-fda-acceptance-and-priority. Accessed December 26, 2022.
33 Over-the-Counter Naloxone One Step Closer as Harm Reduction Therapeutics Initiates a Rolling Submission of its New Drug Application (NDA) to U.S. Food and Drug Administration for RiVive™ (3.0 mg intranasal naloxone) for Emergency Treatment of Opioid Overdose. https://www.prnewswire.com/news-releases/over-the-counter-naloxone-one-step-closer-as-harm-reduction-therapeutics-initiates-a-rolling-submission-of-its-new-drug-application-nda-to-us-food-and-drug-administration-for-rivive-3-0-mg-intranasal-naloxone-for-emergency--301645959.html. Published October 11, 2022. Accessed December 26, 2022.
34 Cohen BR, Mahoney KM, Baro E, et al. FDA Initiative for Drug Facts label for over-the-counter naloxone. New England Journal of Medicine. 2020;382(22):2129-2136. doi:10.1056/nejmsa1912403
35 For the purposes of this analysis, we counted one nasal spray, one prefilled auto-injector, and one vial as a "dose" of naloxone.
36 IQVIA. National Sales Perspectives (NSP). January 2021 - December 2021. Extracted: July 2022.

manufacturers if there was a possibility these doses were counted in IQVIA data. Our analysis is likely an underestimate of the number of doses distributed in 2021. Naloxone is currently distributed by pharmacies, health care facilities, and organizations outside the traditional health care system, including harm reduction organizations, first responders, prisons, and schools and universities.

In combining typical prescription drug distribution data with data regarding naloxone distribution outside of the traditional health care system, we estimate that approximately **16.95 million** doses of naloxone were distributed in the U.S. in 2021. According to typical prescription drug distribution data, **2.64 million** and **6.61 million** doses were distributed to retail pharmacies and other health care facilities, respectively *(Figure 2)*. An estimated **7.7 million** additional doses were distributed outside retail pharmacies and traditional health care facilities; these doses have largely not been captured in typical drug distribution data. Unlike most prescription medical products, a significant proportion of naloxone is not distributed through a pharmacy or other health care facilities. Millions of naloxone doses are distributed to local health departments, harm reduction organizations, first responders, schools, and other community organizations annually. Naloxone that is distributed outside the traditional health care system may not be captured in typical sources of data about medical product distribution.

Figure 2: Naloxone Doses Distributed in 2021 (in millions)



Opioid Settlement Agreements – Provisions for Naloxone

Future naloxone distribution will be affected by opioid settlement agreements *(Table 4)*.[37] As of November 30, 2022, the opioid manufacturers, distributors, and retailers named in lawsuits related to opioid misuse have agreed to settlements with state, local, and tribal governments. Many of these settlements include funding for naloxone access, and some settlements include details regarding naloxone purchase or donation. Other settlements will be distributed according to state-drafted Memoranda of Understanding (MOUs) outlining how the settlement money is intended to be allocated to funds for states, cities, counties, and defined localities. Within these MOUs, provisions for expanding naloxone access are addressed in the following ways:[38]

1. Support "Naloxone Plus" strategies, which work to ensure that individuals who have received naloxone to reverse the effects of an overdose are then linked to treatment programs or other appropriate services.

2. Increase availability and distribution of naloxone and other drugs that treat overdoses for first responders, overdose patients, individuals with OUD and their friends and family members, schools, community navigators and outreach workers, persons being released from jail or prison, or other members of the general public.

3. Provide free naloxone to anyone in the community via public health entities.

4. Provide training and education regarding naloxone and other drugs that treat overdoses for first responders, overdose patients, patients taking opioids, families, schools, community support groups, and other members of the general public.

5. Enable school nurses and other school staff to respond to opioid overdoses, and provide them with naloxone, training, and support.

6. Expand, improve, or develop data tracking software and applications for overdoses/naloxone revivals.

37 Opioid Litigation Global Settlement Tracker. Opioid Settlement Tracker. https://www.opioidsettlementtracker.com/globalsettlementtracker. Accessed December 26, 2022.
38 National Opioid Settlement. https://nationalopioidsettlement.com/. Accessed December 26, 2022.
39 Peet ED, Powell D, Pacula L. Trends in out-of-pocket costs for naloxone by drug brand and payer in the US, 2010-2018. JAMA Health Forum. 2022;3(8):e222663. doi:10.1001/jamahealthforum.2022.2663

Table 4: Summary of Opioid Settlement Agreement Funding for Naloxone

	Settlement	Naloxone Provisions
MANUFACTURERS		
Purdue	Up to **$6 billion**	Per state MOUs
Teva	**$3 million** in cash over 13 years **$240 million** in lieu of naloxone product (determined by state)	**$1.2 billion** in generic naloxone (valued at wholesale acquisition cost) over 10 years **$75 million** in Narcan® to Texas
Allergan/AbbVie	**$2.37 billion**	Per state MOUs
Endo	**$450 million** over 10 years; state-specific settlements	Per state MOUs
DISTRIBUTORS		
J&J, McKesson, Amerisource-Bergen, Cardinal Health combined settlement	**$26 billion** distributed over 18 years; state-specific allocations	Per state MOUs
RETAILERS		
CVS	**$5 billion** over 10 years	**$484 million** over 18 years to the state of Florida Nationwide access in CVS Pharmacy locations to life-saving opioid overdose reversal medication
Walgreens	**$5.7 billion** over 15 years	**$683 million** over 18 years to Florida Naloxone will be available in all Walgreens pharmacies nationwide
WalMart	**$3.1 billion**	Per state MOUs
Rite Aid of MA	**$177,000**	Contributed to the state's naloxone fund
Ride Aid & Giant Eagle	**$2.2 million** allocated to Ohio Lake and Trumbull counties	Per state MOUs

THREE | PAYING FOR NALOXONE DISPENSED IN PHARMACIES

Naloxone costs at retail pharmacies are covered by various payors including, but not limited to: commercial insurance, Medicaid programs, Medicare and Medicare Advantage programs, Veterans Affairs, State and Federal Funding (e.g., SAMHSA grants), or (OOP). Health Savings Accounts (HSAs) and Flexible Spending Accounts (FSAs) may ameliorate naloxone OOP costs for people enrolled in these programs.

Payor coverage and OOP costs for naloxone from 2014-2018 were assessed using pharmacy claims data in an article by Peet, et al. OOP costs increased sharply for the uninsured from 2015 to 2016: "For uninsured patients, the mean OOP cost of Evzio® was 14.9 times the mean OOP cost of Narcan® and 16.02 times the mean OOP cost for generic naloxone."[39] Since then, commercial insurance providers (e.g., Optum) have instituted low- or no-copay programs for naloxone, ensuring that at least one formulation is available at no cost or a discounted price.

Most private insurance plans are required to cover preventive services assigned a United States Preventive Services Task Force (USPSTF) grade A or B without a copay.[41] However, no recommendation for "preemptive prescribing of naloxone for mitigating overdose risk" currently exists.[41] Despite this, the cost of naloxone is generally covered by most insurance policies. All state Medicaid plans reimburse for at least one naloxone formulation, though constraints to obtaining the medication, such as PA requirements, may exist.[42] The Department of Veterans Affairs has eliminated copayment for all opioid antagonists.[43]

Insurance coverage of OTC and nonprescription medications varies from plan to plan. Currently, 49 state Medicaid plans cover OTC and nonprescription medications. Stipulations for coverage may include requiring a prescription written by a licensed provider for the OTC and nonprescription products, PA, or quantity or fill limit policies. OTC and nonprescription medications may be covered by a supplemental benefit of a Medicare Advantage plan.[44]

How naloxone coverage may be affected by a prescription to nonprescription switch was explored during a payor roundtable convened in October 2022 (meeting agenda can be found in the Appendix).

40 USPSTF: Who we are & how we work - United States Preventive Services ... https://www.uspreventiveservicestaskforce.org/uspstf/sites/default/files/inline-files/uspstf-who-we-are-how-we-work_1.pdf. p.6. Accessed December 26, 2022.

41 Chou R, Dana T, Blazina I, Grusing S, Fu R, Bougatsos C. Interventions for Drug Use—Supplemental Report: A Systematic Review for the U.S. Preventive Services Task Force. Evidence Synthesis No. 187. AHRQ Publication No. 19-05255-EF-2. Rockville, MD: Agency for Healthcare Research and Quality; 2020.

42 Substance Abuse and Mental Health Services Administration. Medicaid Coverage of Medication-Assisted Treatment for Alcohol and Opioid Use Disorders and of Medication for the Reversal of Opioid Overdose. HHS Publication No. SMA-18-5093. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2018.

43 Elimination of Copayment for Opioid Antagonists and Education on the Use of Opioid Antagonists. 38 CFR Part 17. October 20,2021.

44 Using the Medicare Advantage Over-the-Counter (OTC) Medicines Program as a Consumer Engagement Tool. Consumer Healthcare Products Association. https://www.chpa.org/about-consumer-healthcare/research-data/research-reports/using-medicare-advantage-over-counter-otc-consumer-engagement. Accessed December 26, 2022.

Payor Roundtable: Considerations for Coverage of Over-the-Counter Medications

The FDA Foundation convened a virtual roundtable meeting to identify factors considered in decision-making processes for whether to include OTC and nonprescription medications as part of health/pharmacy insurance benefits and coverage. This section summarizes the discussion from the meeting of public and private payor representatives and experts (n=11), knowledgeable about the economic implications of medical products transitioning from prescription to nonprescription status. The focus of the meeting was to understand 1) the factors considered when covering nonprescription medications and 2) how these factors may affect consumer access to medication.

The FDA Foundation hosted this conversation with the intention of providing insight to FDA and other federal agencies regarding the payor decision-making process for covering nonprescription medications.

Meeting Findings

Participants shared that payors make nonprescription drug coverage decisions by considering a number of elements, including:

- Legal mandates (e.g., Affordable Care Act requirements),
- Medications recommended as part of USPSTF Grade A and B recommendations,
- Clinical merit,
- Fiscal considerations,
- Relative cost of product (portion of pharmacy benefit budget, rebates, manufacturer incentives),
- Policy implications (particularly program integrity),
- Political climate, and
- Insurance industry standards.

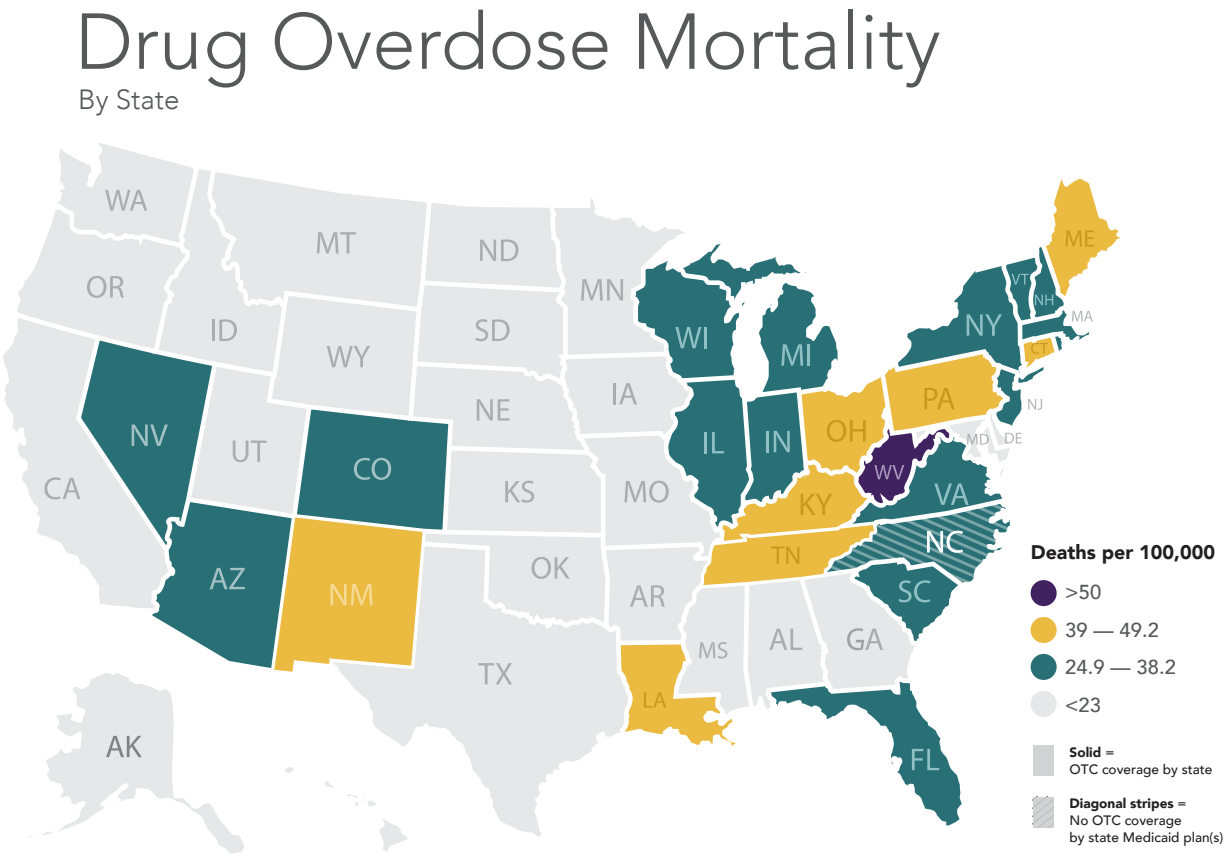
The posture of payors towards OTC and nonprescription coverage has changed over the past decade with the increase in market share of high-cost specialty medications. Today, payors pay particular attention to specialty drug spending, with less of an emphasis on products that may move to nonprescription status. Further, payors are more willing to consider including OTC and nonprescription medications in the pharmacy benefit, particularly life-saving drugs or medications that have off-setting cost benefits. In addition, payors stated that they would likely cover a prescription naloxone formulation if it was a different delivery system from the nonprescription status version, but insurance coverage of nonprescription medications is more complex than direct consumer payment. Technical and logistical issues at the pharmacy, including documentation of the claim, often in the form of a prescription, is often required for program integrity and fraud protection.

Additional considerations of payors include:

1. **State Medicaid Programs:** Although Medicaid coverage of nonprescription medications is optional, 49 state Medicaid programs cover OTC medications (*Figure 3: Drug Overdose Mortality by State and OTC Medication Coverage by State Medicaid Plans*). Providing this coverage requires time (*~3-6 months*) to add an OTC medication. If Federal funds are being used to cover an OTC medication, a prescription from a provider is required for the OTC medication. Coverage is specific to the state and state plans administering Medicaid benefits.

2. **Medicare Programs:** Under current law, Medicare does not pay for OTC medication. No precedent exists for the coverage of a life-saving OTC medication. Medicare Advantage Part D programs (*prescription drug benefits offered under Medicare Advantage*), may, and often do, cover OTC medications. Supplemental benefits may also cover OTC medication; coverage is plan-specific.

Figure 3: Drug Overdose Mortality by State and OTC Medication Coverage by State Medicaid Plans [45]



45 Drug overdose mortality by State. Centers for Disease Control and Prevention. https://www.cdc.gov/nchs/pressroom/sosmap/drug_poisoning_mortality/drug_poisoning.htm. Published March 1, 2022. Accessed January 12, 2023.

FOUR | RX-TO-OTC SWITCH CONSIDERATIONS

Moving medications to OTC status provides consumers access to medication without the time and expense of a health care provider interaction required to obtain a prescription. All stakeholders, including payors, may benefit when consumers can directly access effective treatments. Payors may benefit from eliminating costs for unnecessary clinic visits or testing. In addition, having OTC medication readily available in convenient retail locations and online may help address disparities in access to health care. Conversely, a shift from prescription-only to nonprescription status may create negative consequences when it comes to paying for such products, as the medication cost may switch from a covered insurance benefit to a fully OOP consumer-borne cost.

Insurance Coverage

As discussed by roundtable participants, many private insurance plans, Medicaid, and Medicare Advantage plans include OTC medications in plan benefits. Depending on payor type and payor policies, OTC medications may be partially or wholly covered by the payor. Impact of a naloxone prescription to nonprescription status switch may be minimal if insurance plans deem coverage to be essential and cost-effective. With any potential OTC switch, payors need sufficient time to prepare to ensure access for their beneficiaries/covered lives.

The 2020 CARES Act allows for coverage of OTC medications by HSAs and FSAs. Consumers with these benefits would be able to offset nonprescription naloxone OOP costs.

Full coverage of nonprescription naloxone without a copay or coinsurance facilitates access. Simplifying the purchase process (*e.g., not requiring extra steps such a prescription for the nonprescription formulation or PA*) may also reduce anxiety and stigma associated with buying naloxone. Insured persons may worry about other plan members (e.g., parents, if the covered person is a young adult), employers, or their insurance company becoming aware of the naloxone claim and potential repercussions. Assurance by the health plan that obtaining naloxone is confidential and will not affect overall health care coverage is an important step in breaking down barriers to access.

State mandates for coverage of opioid overdose reversal agents and USPSTF assignment of a Grade A or B recommendation for using naloxone to manage opioid overdose would help ensure national naloxone coverage without cost-shifting to consumers. Such actions also create a basis for combatting stigma – setting standards supporting conversations about overdose and policies to ensure naloxone is immediately available for use by bystanders outside of healthcare settings.

Access and Cost-Shifting to Consumers

Nonprescription naloxone could be sold outside of pharmacies, therefore increasing access and reducing pharmacy deserts. Eliminating these access deficits also helps to reduce the stigma associated with prescribing, dispensing, and carrying naloxone.[47]

Depending on drug price, broader access may be countered by a high OOP cost, becoming cost-prohibitive in areas with the highest need. Part of the difficulty in achieving universal, low-barrier, nonprescription access to naloxone lies in the price to consumers. Nonprescription naloxone nasal spray will likely be costly, even if multiple generics become available to create market competition. Further, approval of nonprescription naloxone via the New Drug Application pathway may provide manufacturers with patent exclusivity, which would limit the potential price competition of generic alternatives.

Beyond pricing and coverage questions, supply chain dynamics will also be affected in a prescription to nonprescription switch.

Supply Chain

The FDA issued guidance regarding the Public Health Emergency exclusion as it applies to the Drug Supply Chain Security Act (DSCSA). This guidance clarifies exemptions from the DSCSA for harm reduction organizations reporting difficulties acquiring naloxone.[47] Approval of nonprescription naloxone products would allow organizations to purchase the medication directly, eliminating barriers which make purchasing naloxone more difficult. It is likely that nonprescription status would more efficiently put naloxone in the hands of people on the front lines of the overdose crisis.

46 Centers for Disease Control and Prevention. Still not enough naloxone where it's most needed. https://www.cdc.gov/media/releases/2019/p0806-naloxone.html. Published August 6, 2019. Accessed December 26, 2022.

47 Exemption and Exclusion From Certain Requirements of the Drug Supply Chain Security Act for the Distribution of FDA-Approved Naloxone Products During the Opioid Public Health Emergency Guidance for Industry. FDA-2022-D-1847. September 22, 2022. https://www.fda.gov/media/161750/download. Accessed December 26, 2022.

Drug Shortages

As access increases with the availability of nonprescription naloxone, the potential for drug shortages should also be considered. More product will be needed to stock shelves in pharmacy and non-pharmacy retailers. State and local programs currently providing naloxone are not able to keep up with demand, and it is imperative that product shortages do not compound this problem.[48,49] How the opioid settlements will affect naloxone supply remains to be seen. Teva, CVS, Walgreens and Rite Aid of MA settlements contain provisions for naloxone distribution, and states' funding for access to nonprescription naloxone purchase will also increase. Higher demand must be met with the adequate supply for nonprescription naloxone to truly improve.

FIVE | CONCLUSION

Naloxone is an important public health tool that should be available to anyone in the position to assist someone experiencing opioid overdose. A prescription to nonprescription switch is a potential mechanism to expand naloxone availability, although nonprescription naloxone alone is not the sole solution to expanding access. Such a switch should be a component within the context of a larger strategy addressing expanded distribution, insurance coverage, cost to the consumer, and production keeping pace with high demand.

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REAGAN-UDALL FOUNDATION
for the Food and Drug Administration

Considerations for Coverage of Over-the-Counter Medications

Virtual Roundtable

October 25, 2022 from 12:30 – 3 p.m. Eastern Time

AGENDA

Meeting Purpose: Explore factors considered in decision-making processes for whether to include over-the-counter (OTC) medications as part of health/pharmacy insurance benefits and coverage. This virtual, invitation-only roundtable will include a variety of public and private payor representatives and experts to discuss the economic implications of medical products transitioning from prescription to OTC status.

Background:

A potential shift in prescription-only to OTC status for medications requires consideration on the part of sponsors/manufacturers, regulators, payors, health professionals, and consumers. In recent years, there have been efforts to increase access to certain drugs at both the state and federal level. Examples include shifting products from prescription to nonprescription (or OTC) status or expanding eligible individuals and circumstances for prescribing medications (*e.g., oral contraceptives, naloxone, and insulin*) and devices (*e.g., COVID-19 test kits and hearing aids*). Moving medications to OTC status provides consumers access to medication without the time and expense of a health care interaction required to obtain a prescription. All stakeholders, including payors, may benefit when consumers can directly access effective treatments. Payors may benefit from not having to pay for unnecessary clinic visits or testing. In addition, having OTC medication readily available in convenient retail locations, and online, may help address disparities in access to health care. However, a shift from prescription-only to OTC status may create negative consequences when it comes to paying for such products, as the medication cost may switch from a covered insurance benefit to a fully out-of-pocket cost. (*Although conversion to nonprescription status does not always equate with a shift to uncovered status: some state Medicaid plans as well as Medicare Advantage plans, cover some OTC medications.*)

This conversation is intended to provide insight to FDA and other federal agencies regarding the payor decision-making process for covering nonprescription medications.

12:30 p.m. **Welcome and 'Ground Rules'**

Speaker: Susan C. Winckler, RPh, Esq, Chief Executive Officer, Reagan-Udall Foundation for the FDA

12:35 p.m. **Opening Remarks from U.S. Food and Drug Administration**

Speaker: Marta Sokolowska, Deputy Center Director for Substance Use and Behavioral Health, Center for Drug Evaluation and Research

12:40 p.m. **The Changing Consumer Landscape**

Speaker: Winckler

12:50 p.m. **Participant Introductions**

Moderator: Winckler

When called on, please share your name, affiliation, and role within your organization. (*Please keep your introductions to ~30 seconds each.*)

1 p.m. **Group Discussion**

Moderator: Winckler

Key Question:

- What factors do payors consider when deciding when and at what level to include OTC medications as part of a pharmacy benefit?

Scenarios to Explore:

- Under what circumstances are payors required to cover OTCs? If not required, when would payors typically cover OTCs voluntarily?
- When a product has both prescription and OTC options, how does that factor into coverage decisions?
- If one dosage form is OTC but another dosage form is prescription, how might that impact coverage decisions?
- If the insured individual is given an OTC medication during inpatient care, and that OTC medication needs to be continued in the outpatient setting, how does that impact the outpatient OTC medication coverage decisions?
- What are the considerations for medical products that payors cover with no copay that transition from prescription-only to OTC?

2:50 p.m. **Next Steps**

Speaker: Winckler

3 p.m. **Adjournment**

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