



Naloxone for Opioid Overdose: Regulation and Policy Options

In the United States, the annual number of drug overdose deaths involving opioids has more than quadrupled since 1999, according to the Centers for Disease Control and Prevention (CDC). Recent estimates (through the third quarter of 2016) show that the age-adjusted rate of drug overdose deaths has continued to rise. Research published in the *American Journal of Preventive Medicine* finds that the proportion of drug overdose deaths involving opioids has been underestimated (Ruhm 2017). The prescription drug naloxone is currently the “only safe and appropriate treatment” for opioid overdose, according to the Substance Abuse and Mental Health Services Administration (SAMHSA) Opioid Overdose Prevention Toolkit.

How Naloxone Works

The drugs commonly called opioids—whether prescription drugs (e.g., oxycodone) or street drugs (e.g., heroin)—are opioid *agonists*, meaning they bind to and activate opioid receptors in the brain. Opioids relieve pain, may induce euphoria, and have other effects such as depressing both the central nervous system and the respiratory system. In the event of an overdose, these latter effects may manifest in a range of physical problems, including severe drowsiness, dangerously slow breathing, coma, and even death.

Naloxone is an opioid *antagonist*, meaning it binds to opioid receptors but does not activate them. When administered during an opioid overdose, naloxone temporarily displaces opioid agonists from the opioid receptors and blocks additional opioid agonists from binding to the opioid receptors. By temporarily displacing and blocking opioid agonists, naloxone temporarily stops their effects, thus reversing the overdose.

SAMHSA’s Opioid Overdose Prevention Toolkit includes five steps for first responders to take in the event of an opioid overdose: (1) call for help (dial 911), (2) check for signs of opioid overdose, (3) support the individual’s breathing, (4) administer naloxone, and (5) monitor the individual’s response.

Policy Problem: Access Is Limited

Concern about opioid overdose deaths has led many people, including the members of the President’s Commission on Combating Drug Addiction and the Opioid Crisis, to call for increased access to naloxone. Comparatively few people oppose expanded access to naloxone, arguing that such efforts implicitly condone opioid abuse. Naloxone must often be administered by lay people outside a medical setting (as described above); however, until recently naloxone was available only in an injectable form, which may be difficult for a lay person to administer (see “Dosage Form” in the next column). Also, naloxone is currently available by prescription only, which limits access (see “Prescription Requirement” in the next column).

Federal Regulation of Naloxone

Naloxone is regulated under the Federal Food, Drug, and Cosmetic Act (FFDCA, 21 U.S.C. §§301 et seq.), which gives the Food and Drug Administration (FDA) in the Department of Health and Human Services (HHS) primary responsibility for ensuring the safety and effectiveness of drugs, regardless of whether they are controlled substances. See CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*. Naloxone is not known to carry risk of addiction and is not regulated under the federal Controlled Substances Act.

Representatives of the FDA and other HHS agencies have publicly discussed two major options for increasing access to naloxone: (1) making naloxone available in easier-to-administer forms and (2) making naloxone available without a prescription.

Dosage Form

For more than 40 years, naloxone was available only in an injectable form, which is difficult for nonprofessionals such as friends or family members to administer. Further, both medical professionals and nonprofessionals are at risk of accidental needle sticks when giving injections. In recent years, the FDA has approved naloxone in forms that are easier to administer.

Table 1. Naloxone: Dosage Form

Dosage Form	Sold As	Year Approved
Injectable	naloxone (generic)	1971
Auto-injector	Evzio®	2014
Nasal spray	NARCAN®	2015

Source: Data publicly available from the FDA’s Orange Book.

Notes: Injectable naloxone is available as a generic drug marketed by multiple manufacturers: Evzio® is a registered trademark of Kaléo, Inc., and NARCAN® is a registered trademark of Adapt Pharma Operations Limited.

Prescription Requirement

Naloxone is currently available only by prescription. The FFDCA offers two mechanisms by which naloxone could become a nonprescription (over-the-counter) drug. One mechanism is the submission of a new drug application (NDA) or a supplemental NDA, which would have to be submitted by the manufacturer. The other mechanism is via rulemaking pursuant to 21 C.F.R. §310.200(b), which allows a prescription exemption when the Commissioner of Food and Drugs finds that prescription-dispensing requirements are unnecessary for safe and effective use of a drug in self-medication (as directed by proposed labeling). This process may be initiated by the commissioner or any interested person (i.e., a citizen petition).

Options in Health Policy

Many recent efforts to increase access to naloxone have been undertaken by states or local communities. Indeed, one of the recommendations from the President's Commission is that the Administration should provide model legislation that states would be able to enact. A common strategy at the federal level is to provide support for state and local initiatives through grants or technical assistance. Accordingly, many of the options described below involve changes to state law.

Third-Party Prescriptions

Laws allowing third-party prescriptions provide an exception to the usual requirement in state law that prescriptions be written only for the person who will actually take the medication. These laws allow prescriptions to be written for a family member or friend of an at-risk individual, rather than the individual himself or herself.

Standing Orders

Some states have, in effect, made naloxone available without a prescription from the patient's perspective through standing orders. When a prescriber issues a standing order for naloxone, the drug may be dispensed to a patient based on a set of criteria, without the prescriber having examined the patient. Some states achieve a similar result using a different mechanism: they have laws authorizing pharmacists to dispense naloxone without a prescription following a specified protocol.

Distribution Programs

Some state- and community-based programs have developed kits containing injectable naloxone, mucosal atomization devices, and instructions for converting the injectable naloxone into a nasal spray. Laws establishing naloxone distribution programs formalize a process for training individuals at risk of opioid abuse and/or their family members or friends, as well as providing them with naloxone kits.

Educational Strategies

Laws requiring educational strategies establish requirements for educational activities beyond naloxone distribution programs. For example, they may require pharmacists dispensing naloxone pursuant to a standing order or protocol to provide certain instructions.

Other Potential Health Policy Options

The policy options above represent established practices that more states might be encouraged to adopt. Other recommendations are less well-established. For example, some recommendations focus on reducing the cost of naloxone to patients by mandating insurance coverage of the drug, reducing the cost of naloxone to government entities (e.g., state Medicaid agencies) by negotiating with the manufacturers, or reducing the cost of naloxone to state and local entities by providing federal funds. The President's Commission also recommends adopting policies to encourage prescribers to co-prescribe naloxone along with opioid prescriptions, as well as exploring options for

notifying physicians of patients who have been revived with naloxone when experiencing an opioid overdose.

Options in Law Enforcement Policy

As with health policy, law enforcement policy related to naloxone has largely been undertaken by states or local communities. The federal role may be to encourage or facilitate state and local efforts.

Equipping Law Enforcement with Naloxone

Federal grants may support state and local efforts to equip law enforcement officers with naloxone. In addition, federal grants and/or technical assistance may support training in how to administer naloxone.

911 Good Samaritan Laws

Victims and witnesses of overdoses may hesitate to call 911 for fear of criminal prosecution on drug charges. Laws providing immunity for those who act in good faith to seek medical care may allay such fears and increase treatment-seeking behavior. A variation on 911 Good Samaritan laws allows judges to consider a good-faith 911 call as potentially mitigating any sentencing for an overdose witness who is criminally prosecuted.

Liability Protections

Laws establishing liability protections alleviate concerns of prescribers or lay people acting in good faith. Such laws may protect professionals who prescribe, dispense, or administer naloxone from criminal or civil liability. Similar laws may protect lay people who distribute naloxone kits or administer naloxone from criminal or civil liability.

Related Federal Grant Programs

While many federal grant programs with broad purposes might potentially allow grantees to use funds to support access to naloxone, the Comprehensive Addiction and Recovery Act of 2016 (CARA, P.L. 114-198) authorized several programs that explicitly address overdose reversal:

- Grants for Reducing Overdose Deaths (42 U.S.C. §290dd-3)
- Opioid Overdose Reversal Medication Access and Education Grant Programs (42 U.S.C. §290ee)
- First Responder Training (42 U.S.C. §290ee-1)
- State Demonstration Grants for Comprehensive Opioid Abuse Response (42 U.S.C. §290ee-3)
- Comprehensive Opioid Abuse Grant Program (42 U.S.C. §3797ff et seq.)

Note that authorized grant programs might not receive funding in a given year. Also, funded grants accept applications only during defined periods. Search the Catalog of Federal Domestic Assistance (www.cfda.gov) or www.grants.gov to find specific grant opportunities.

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