

# NALOXONE FOR OVERDOSE PREVENTION

## PRESCRIBING GUIDANCE FOR CLINICAL SETTINGS

### SUMMARY

Prescribe naloxone to your patients with these risk factors for opioid overdose:

1. High-dose opioid prescription ( $\geq 90$  total morphine milligram equivalents/day)
2. Chronic opioid therapy ( $\geq 3$  months)
3. Opioid\* misuse/illicit use, including:
  - a. Current or past history
  - b. In treatment for opioid use disorder (e.g., methadone, buprenorphine, naltrexone, treatment without pharmacotherapy)
  - c. Opioid overdose history
4. Family member or friend of a person who meets the above criteria

*\*Refers to all opioid drug types (e.g., opioid analgesic prescription, heroin) and all routes of administration (e.g., injection drug use, oral, intranasal)*

For patients who meet any of criteria 1-3, **additional risk** can be conferred by:

**Decreased tolerance after a period of abstinence (e.g., incarceration, hospitalization, detoxification).**

Opioid use after periods of abstinence such as after incarceration, and the resulting loss of tolerance substantially increases risk for overdose. Overdose is a leading cause of death after incarceration.<sup>1,2</sup> The period of abstinence and resulting loss of tolerance associated with incarceration, hospitalization and detoxification is likely the underlying reason for elevated overdose risk.<sup>1</sup>

**Concurrent use of central nervous system (CNS) depressants (e.g., benzodiazepines, alcohol):**

Concurrent use of opioids and CNS depressants, such as benzodiazepines and alcohol, increase the risk for overdose.<sup>3-8</sup>

### BACKGROUND

Overdose deaths from opioid analgesics and heroin are a public health crisis in Philadelphia. In 2020, the majority (85%) of overdose deaths involved an opioid. Fentanyl contributes to the vast majority of these deaths, though heroin and prescription opioids are also found in the toxicology of overdose decedents in Philadelphia. These overdose deaths are preventable, using a comprehensive approach that includes prevention, treatment of opioid use disorder and raising public awareness. Because most overdoses are witnessed by

another person,<sup>10</sup> a key strategy to prevent opioid overdose deaths is to increase access to naloxone – an antagonist medication that reverses an opioid overdose. In many states, including Philadelphia, legislation allows trained lay-people to carry and use naloxone as a first-aid response for an overdose. This strategy is effective. Nationally, since 1996, more than 150,000 individuals have received naloxone through community-based programs, and more than 26,000 overdose reversals have been reported.<sup>11</sup> A landmark Massachusetts study

demonstrated reduced opioid overdose death rates in communities with naloxone distribution programs.<sup>12</sup>

In clinical settings (e.g., primary care practices, emergency departments), naloxone has not been routinely prescribed to patients for overdose prevention, but is more commonly administered by health care professionals for acute, on-site overdose reversals. Prescribing naloxone for overdose prevention to at-risk patients can have a two-fold benefit: the naloxone could be used to reverse an overdose experienced by the

patient, or the patient could use it to reverse an overdose that they witness. Prescribing naloxone to family members or friends of at-risk individuals can further expand the impact of this life-saving medication.

This guidance can help clinicians prescribe naloxone for overdose prevention; it includes the Philadelphia Department of Public Health's suggested criteria for determining which patients should be offered a naloxone prescription and the evidence for these criteria.

## GUIDANCE

PDPH recommends offering naloxone to patients with the following risk factors for an opioid overdose. These criteria are based on review of the scientific literature, other published naloxone prescribing guidance and expert opinion.<sup>13-17</sup>

### **1. High-dose opioid prescription ( $\geq 90$ total morphine milligram equivalents/day):**

Risk of opioid over-dose and overdose death increases with higher opioid analgesic dosages.<sup>18-20</sup> There is significantly increased risk for fatal overdose at  $\geq 90$  morphine milligram equivalents (MME) per day.<sup>18-20</sup> To quickly calculate MME for patients, use CDC Opioid Guideline Mobile App a free CDC app available through Apple and Google Play stores, specifically developed to assess overdose risk based on total daily MME. If dosing does reach  $\geq 90$  MME/day, thoroughly reassess the relative risks and harms versus pain and functional benefits, and consider reducing the dose if unfavorable. Offer naloxone for overdose prevention.<sup>20</sup>

**2. Chronic opioid therapy ( $\geq 3$  months):** Chronic opioid therapy ( $\geq 3$  months) for chronic non-cancer pain is associated with increased risk for overdose. Several factors might explain this observation. Individuals taking chronic opioid therapy might be taking higher dosages, and higher dosages are associated with increased overdose risk.<sup>18, 19</sup> Additionally, these individuals might be more likely to take long-acting opioids, a formulation which confers a greater risk for overdose.<sup>21</sup> Risks and benefits of prescribing chronic opioid therapy should be weighed carefully. For patients on chronic opioid therapy, a naloxone prescription can be offered for overdose prevention.

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**3. Opioid\* misuse or illicit use, including:**

**a. Current or past history:** Current and past history of illicit opioid use<sup>22</sup> and/or opioid analgesic misuse are risk factors for overdose.<sup>23</sup> All routes of opioid administration can confer overdose risk, although injection drug use is associated with the greatest risk.<sup>24</sup> One meta-analysis demonstrated that cohorts with higher injection prevalence had a higher overdose mortality rate (0.83 per 100 person-years) as compared to cohorts with low injection prevalence (0.33 per 100 person-years).<sup>25</sup>

**b. In treatment for opioid use disorder:** Several modalities are used to treat opioid use disorder, including pharmacotherapy and treatment without pharmacotherapy. Pharmacotherapy with opioid agonists (methadone and buprenorphine) is the most effective form of treatment; in clinical trials, treatment with opioid agonist therapy is superior to treatment without.<sup>26, 27</sup> Opioid agonist therapy decreases drug use and mortality.<sup>26-29</sup> Another pharmacotherapy option is the opioid antagonist naltrexone. For individuals who have a history of any treatment for opioid use disorder, periods out of treatment are associated with risk of relapse and overdose. In one study, the mortality rate was more than twice as high during out-of-treatment versus in-treatment periods; the risk of death was particularly pronounced in the first month after stopping treatment, with a mortality rate more than eight times higher during this period versus the mortality rate during the stable period of treatment. Offering naloxone to patients receiving any treatment modality can reduce future overdose risk.

**c. Opioid overdose history:** Previous history of an opioid overdose is a strong predictor of risk for subsequent overdose.<sup>5, 30, 31</sup> In one survey of drug users, history of previous overdose nearly doubled the risk of experiencing an overdose in the past year.<sup>31</sup>

**4. Family member or friend of an individual who meets criteria:** Family members or friends of an individual who meets any of the above criteria can also be offered a naloxone prescription since they may witness an overdose. Additionally, a statewide standing order for naloxone allows all Pennsylvanians to request naloxone from their pharmacy without an individual prescription. Under the Pennsylvania Naloxone Co-pay Assistance Program, residents who purchase naloxone using their insurance may be eligible to receive up to \$75 from the Department of Aging to assist with the reimbursement of naloxone.

Naloxone is an important component of a comprehensive approach to reducing opioid overdose, along with effective treatment, judicious opioid prescribing, public awareness and community initiatives. By offering naloxone for overdose prevention to patients at risk of opioid overdose and their family and friends, Philadelphia care providers can help prevent overdose mortality.

For more information,  
check out [phillynaloxone.com](http://phillynaloxone.com) or contact [overdose.prevention@phila.gov](mailto:overdose.prevention@phila.gov).

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