

# Naloxone for Overdose Prevention

## Prescribing Guidance for Clinical Settings

### Summary

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

1. High-dose opioid prescription ( $\geq 100$  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 an individual who meets 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 the presence of:**

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

Opioid use after periods of abstinence, such as after incarceration, 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 risk for overdose.<sup>3,4,5,6,7,8</sup>

### Background

Overdose deaths from opioid analgesics and heroin are a public health crisis in New York City (NYC). In 2013, the majority (77%) of overdose deaths involved an opioid. Between 2000 and 2013, opioid analgesic overdose deaths increased 256%, from 0.9 to 3.2 deaths per 100,000 New Yorkers. Between 2010 and 2013, heroin overdose deaths doubled from 3.1 to 6.2 deaths per 100,000 New Yorkers.<sup>9</sup> 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,<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 New York, legislation allows trained laypeople to carry and use naloxone as a first-aid response for an overdose. This strategy is effective. Nationally, since 1996, >150,000 individuals have received naloxone through community-based programs, and >26,000 overdose reversals have been reported.<sup>11</sup> A landmark Massa-

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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 he/she witnesses. 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 NYC Department of Health and Mental Hygiene's (DOHMH's) suggested criteria for determining which patients should be offered a naloxone prescription and the evidence for these criteria.

## Guidance

DOHMH 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, 14, 15, 16, 17</sup>

- 1. High-dose opioid prescription ( $\geq 100$  total morphine milligram equivalents/day):** Risk of opioid overdose and overdose death increases with higher opioid analgesic dosages.<sup>18, 19</sup> Taking  $\geq 100$  morphine milligram equivalents (MME) per day is associated with seven times the risk for overdose death compared with patients taking  $< 20$  MME.<sup>18</sup> DOHMH recommends 100 total daily MME as a threshold for caution and patient reassessment.<sup>20</sup> To quickly calculate MME for patients, use OpioidCalc, a free DOHMH app for iOS and Android, specifically developed to assess overdose risk based on total daily MME. If total daily MME is  $\geq 100$ , consider tapering the dosage and/or trying alternative treatments for pain; offer naloxone for overdose prevention.
- 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. The most recent reviews on the topic find insufficient evidence that chronic opioid therapy for chronic non-cancer pain improves pain or function.<sup>22, 23, 24, 25, 26</sup> For patients on chronic opioid therapy, a naloxone prescription can be offered for overdose prevention.

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### 3. Opioid\* misuse/illicit use, including:

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

**a. Current or past history:** Current and past history of illicit opioid use<sup>27</sup> and/or opioid analgesic misuse are risk factors for overdose.<sup>28</sup> All routes of opioid administration can confer overdose risk, although injection drug use is associated with the greatest risk.<sup>29</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>30</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>31, 32</sup> Opioid agonist therapy decreases drug use and mortality.<sup>31, 32, 33, 34</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.<sup>33</sup> 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, 35, 36</sup> In one survey of drug users, history of previous overdose nearly doubled the risk of experiencing an overdose in the past year.<sup>36</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. In a clinical setting, the family member or friend may be the patient or may be accompanying a patient to a visit. New York State Public Health Law provides liability protection for prescribing naloxone to non-patients when the institution or practice is registered as an opioid overdose prevention program. Any hospital or doctor's office can register.\*

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, New York City health care providers can help prevent overdose mortality. NYC DOHMH offers technical assistance, and educational materials

For more information, contact [naloxoneprescribing@health.nyc.gov](mailto:naloxoneprescribing@health.nyc.gov).

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