



Prevention of Fatalities from Opioid Overdose: Prescribing Naloxone in the Outpatient Setting

Clinical Practice Guideline

“These guidelines are provided to assist physicians and other clinicians in making decisions regarding the care of their patients. They are not a substitute for individual judgment brought to each clinical situation by the patient’s primary care provider-in collaboration with the patient. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication, but should be used with the clear understanding that continued research may result in new knowledge and recommendations”.

Background / General Principles:

Opioid abuse and overdose is a major public health problem locally and nationally; rates of both abuse and overdose have skyrocketed recently. In 2014, 303 people died from drug overdose in Baltimore alone (more than from homicide)¹. In both Washington DC and Maryland, the estimated death rate is between 18.6 and 21 deaths per 100,000². Nationally, the CDC reported that opioids were involved in more than 33,091 deaths in 2015, with the rate of overdose having quadrupled since 1999.²

As physicians, we are uniquely positioned to be able to intervene on a number of levels to prevent death from opioid overdose; this guideline focuses specifically on the use of prescription naloxone to treat opioid overdose.

Routine prescribing of naloxone to patients at risk for opioid overdose is publically supported by:

- The AMA (American Medical Association)
- The ASAM (American Society of Addiction Medicine),
- AAPCC/AACT/ACMT (American Association of Poison Control Centers / American Academy of Clinical Toxicology / American College of Medical Toxicology)
- The National Guideline Clearinghouse—“strong” recommendation

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Patients at risk for opioid overdose: 1,3,4

Please note that some of these characteristics would put patients in violation of the chronic narcotics contract; *always consider safely ceasing to prescribe narcotics to patients in violation of the contract.*

- Patients who have a history of IV drug use or misuse of prescription opioids
- Patients who are receiving opioids from multiple physicians
- Patients who are on a regimen of multiple different opioids
- Patients who use opioids in conjunction with antidepressants, benzodiazepines or alcohol
- Patients with a history of prior overdose
- Patients who are being treated for a substance abuse disorder
- Patients who are active substance abusers, not in treatment
- Patients who use opioids and have mental illness
- Patients who take opioids and have a major organ dysfunction (renal, hepatic, cardiac, pulmonary)
- Patients receiving high dose opioids (see below)

While there is no absolute cutoff to define a daily dose that would indicate a need for naloxone prescription, the literature shows that patients taking 100 mg oral morphine equivalents (OME) per day or higher are almost **9 times** as likely to overdose compared to a "standard" dose of 1-20 OME per day⁵. Patients taking 50-99 OME per day were almost **4 times** as likely to overdose compared to the standard dose⁵.

Approximate **daily** doses equal to 50 mg and 100 mg oral morphine equivalents

Medication	50 mg OME	100 mg OME
Fentanyl TD (Duragesic)	20 mcg	40 mcg
Methadone	12 mg	20 mg
Hydromorphone (Dilaudid)	12.5 mg	25 mg
Oxymorphone (Opana, Numorphan)	16.5 mg	33 mg
Oxycodone (Oxycontin)	33.5 mg	67 mg
Hydrocodone (Vicodin, Norco)	50 mg	100 mg
Tramadol (Ultram)	250 mg	500 mg

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Recommendations^{1,3,4,5,8}:

-Physicians are strongly encouraged to prescribe naloxone for patients taking more than 50 mg OME daily or higher (see table above).

-Physicians are strongly encouraged to prescribe naloxone for any patient taking opioids at any dose who have one or more of the above risk factors.

-ED physicians are strongly encouraged to prescribe naloxone for patients who present to the ED with opiate overdose.

Naloxone Overview:

- Opioid antagonist that competes for the opioid receptor with strongest affinity for the mu receptor.
- Has been used in emergency settings for over 40 years.
- Often used by EMT's and other emergency non-physician personnel.
- FDA approved formulations include IV and IM injections (including an auto-injector) and an intranasal formulation.
- Works quickly (within 1-2 minutes if given iv; 2-5 minutes if given IM or SC and 8-13 minutes if given intranasally) and lasts on average 30-90 minutes. **Note that repeated administration is often necessary, since the half life of naloxone is much shorter than that of most opioids.**⁹ Consequently, EMS should be called immediately when naloxone is given.
- Adverse effects rare³:
 - Most common are acute opiate withdrawal (unpleasant but almost never fatal)
 - Most serious include:
 - Seizures, occurring in 0.6% and causing death in 0.2% of cases
 - Pulmonary edema, occurring in 1.5% and causing death in 0.2% of cases
 - Pneumonia, occurring in 0.3% and causing death in 0.3% of cases
 - Cardiovascular arrest, occurring in 1.7% and causing death in 0.9% of cases

Note, general consensus is that the above fatal events may be due to the overdose rather than the naloxone. It is clear that naloxone markedly decreases fatalities from opioid overdose.

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Naloxone Formulations

(adapted from the Medical Letter, June 5, 2017 and UpToDate Sept 2017)^{10,13}

Drug	Formulations	Usual Dose	Cost (wholesale cost for a single dose)	How supplied
Parenteral generic Naloxone	0.4 mg/ml vials and syringes; 1 mg/ml syringes; 2 mg/2 ml prefilled syringes	0.4-2 mg IV, IM or SC Used with mucosal atomization device intranasally	\$13.70 \$39.60	1 ml vial 2 ml syringe
Evzio (autoinjector)	0.4, 2 mg/0.4 ml prefilled autoinjectors	0.4 or 2 mg IM or SC	\$1875.00	2 auto- injectors per pack
Narcan nasal spray (Adapt)	4 mg/0.1 ml nasal spray	4 mg intranasally	\$62.50	2 nasal spray devices per carton

Insurance coverage

For both DC and Maryland Medicaid, generic naloxone and narcan nasal spray are preferred.

For other insurers, preferred formulations and co-pays vary.

-MedStar Pharmacies at MWHC, MGUH, MFSMC, MUMH, MGSB, MHH and Leisure World stock naloxone and will provide education to patients and care givers

Prescribing

As of June 2017, pharmacies in the state of Maryland may dispense naloxone to any person without a prescription and irrespective of training on use (based on a state-wide standing order)

Intramuscular:

Rx = Naloxone injection 0.4mg/1ml vial
and 3cc, 23g, 1 inch syringes

Unit: 1 ml vial

Disp: two vials

Refill = PRN

Intranasal:

Rx = Naloxone 1mg/ml needless syringe
and intranasal mucosal atomizer device

Unit: 2 ml vial

Disp: two vials

Refill = PRN

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Sig: For suspected opioid overdose, inject 1ml IM in deltoid or thigh, may repeat after 3 minutes if no or minimal response.

Sig: For suspected opioid overdose, spray 1ml in each nostril, may repeat after 3 minutes if no or minimal response.

Intranasal:

Rx= Narcan nasal spray

Unit: 4 mg

Disp: one carton (2 devices)

Refill= PRN

Sig: For suspected opioid overdose, spray the contents of one device in either nostril, may repeat after 3 minutes if no or minimal response

Auto-injector:

Evzio® (naloxone HCl) 0.4mg

Qty: 1 two-pack

Refill: prn

Sig: Inject one vial into the upper-outer thigh for suspected opioid overdose; may repeat after 3 minutes if no or minimal response.

-Please note, the prescription may be written for the patient (and likely administered by a 3rd party) Or it may be prescribed directly to a significant other who will administer it to the patient

Training Resources

It is important to train the patient along with significant others and those likely to be in close proximity during a potential overdose. See below for some training options.

Please note that patients must present to the Emergency Department after using naloxone, as it is relatively short-acting; this point must be stressed during patient education.

- <http://starport.medstar.net/msh/Pharmacy/Pages/default.aspx>
- NYC department of health training video: <https://vimeo.com/4495088>
- <https://bha.health.maryland.gov/NALOXONE/Pages/Core-Curriculum.aspx>
- <http://www.getnaloxonenow.org/>
- <http://prescribetoprevent.org/>
- <https://bha.health.maryland.gov/NALOXONE/Pages/Naloxone.aspx>

Legal considerations:

- Naloxone is FDA-approved for treatment of opioid overdose; physicians need not worry about legal risks.⁸
- Studies have not shown an increase in abuse or in overdose with naloxone prescriptions.^{8,9}
- Good Samaritan laws cover lay people who intervene and administer naloxone.
- Legal precedent of 3rd party emergency administration—epinephrine injection pens for anaphylaxis.

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