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 Washington DC, the estimated death rate is between 12 and 13 deaths per 100,000 (compared to around 11 for Maryland)\(^2\). Nationally, the CDC reported more than 16,000 deaths from opioid overdose in 2013\(^2\).

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
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 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 day\(^5\). Patients taking 50-99 OME per day were almost 4 times as likely to overdose compared to the standard dose\(^5\).

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

<table>
<thead>
<tr>
<th>Medication</th>
<th>50 mg OME</th>
<th>100 mg OME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl TD (Duragesic)</td>
<td>20 mcg</td>
<td>40 mcg</td>
</tr>
<tr>
<td>Methadone</td>
<td>12 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Hydromorphone (Dilaudid)</td>
<td>12.5 mg</td>
<td>25 mg</td>
</tr>
<tr>
<td>Oxymorphone (Opana, Numorphan)</td>
<td>16.5 mg</td>
<td>33 mg</td>
</tr>
<tr>
<td>Oxycodone (Oxycontin)</td>
<td>33.5 mg</td>
<td>67 mg</td>
</tr>
<tr>
<td>Hydrocodone (Vicodin, Norco)</td>
<td>50 mg</td>
<td>100 mg</td>
</tr>
<tr>
<td>Tramadol (Ultram)</td>
<td>250 mg</td>
<td>500 mg</td>
</tr>
</tbody>
</table>
**Recommendations**:\(^1,3,4,5,8\):

- Physicians are strongly encouraged to prescribe naloxone for patients taking 50-100 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 new auto-injector).
- Intranasal use off-label, but well-studied and validated.
- Works quickly (within seconds to minutes) and lasts on average 30-90 minutes.
- Adverse effects rare\(^3\):
  - 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.

**Cost**:

Maryland:
- Generic naloxone has a $1 co-pay for Maryland Medicaid patients
-Starting 10/1/15, the mucosal atomizer (needed for intranasal use) will be covered with this co-pay
-Pharmacies may not deny treatment to a patient who is unable to pay.
-There is no need for a Medicaid prior authorization in Maryland.

Washington D.C.:
- Generic naloxone has a $1 co-pay for Fee For Service Medicaid patients
- Managed Care Organizations (MCO) Medicaid co-pays vary; prior authorization sometimes required.
- Mucosal atomizer typically not covered with co-pay for generic naloxone and usually requires prior authorization.

-Evzio® auto-injector costs around $600

-Please encourage your local pharmacy to stock naloxone.

-Washington D.C.:
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-Please encourage your local pharmacy to stock naloxone.

-MedStar Pharmacies at MWHC, MGUH, MFSMC, MUMH, MGS, MHH and Leisure World stock naloxone and will provide education to patients and care givers
-If you encounter any difficulties, please contact Rajani Gudlavalleti, Director, Baltimore City Opioid Overdose Prevention and Response at Rajani.Gudlavalleti@BaltimoreCity.gov

**Writing the prescription:**

**Intramuscular:**
Rx = Naloxone injection 0.4mg/1ml vial and 3cc, 23g, 1 inch syringes
Unit: 1 ml vial
Disp: two vials
Refill = PRN
Sig: For suspected opioid overdose, inject 1ml IM in shoulder or thigh, may repeat after 3 minutes if no or minimal response.

**Intranasal:**
Rx = Naloxone 1mg/ml needless syringe and intranasal mucosal atomizer device
Unit: 2 ml vial
Disp: two vials
Refill = PRN
Sig: For suspected opioid overdose, spray 1ml in each 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
  -The significant other MUST complete a training program from an authorized entity before having the prescription filled

Instructions to patient and significant others:

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.

-In-office training by physician or nursing staff
- NYC department of health training video: [https://vimeo.com/4495088](https://vimeo.com/4495088)
- [prescribetoprevent.org](http://prescribetoprevent.org) has resources for training

Legal considerations:

-Naloxone is FDA-approved for treatment of opioid overdose; physicians need not worry about legal risks.\(^8\)
-Studies have not shown 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.

References:

2. CDC.gov
6. prescribetoprevent.org.

<table>
<thead>
<tr>
<th>Initial Approval Date and Reviews:</th>
<th>Most Recent Revision and Approval Date:</th>
<th>Next Scheduled Review Date:</th>
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<td>September 2015</td>
<td>September 2015</td>
<td>September 2017 Ambulatory Best Practice</td>
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