Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee, and the Drug Safety and Risk Management Advisory Committee

17-18 December 2018
Agenda

• **Role of Naloxone in the Opioid Overdose Public Health Crisis**

• **Expanded Access to Naloxone**
  – Risk Factors
  – Universal Precautions

• **Naloxone Implementation**
  – Challenges and Recommendations
Responding to a Dynamic Public Health Crisis

Prescribed opioids
Co-prescribing take-home naloxone to patients on opioid analgesics or medication assisted treatment (MAT)\textsuperscript{1-3}

Opioid Use Disorder (OUD)
Patients who are being treated for OUD and their family members/significant others should be given prescriptions for naloxone and trained in the use of naloxone in overdose\textsuperscript{3}

Heroin
Overdose education and naloxone distribution to opioid users and their families and peers\textsuperscript{4}

Synthetic opioids
Illicit fentanyl and fentanyl analogs can trigger rapid onset and progression of overdose: prompt treatment with multiple naloxone doses may be required to reverse overdose\textsuperscript{5}

Opioids and Chronic Diseases

Chronic Pain

- 5-8 million patients rely on opioids for long term management of pain
- 25% decline in total number of opioid prescriptions dispensed 2012-2017

Opioid Use Disorder (OUD)

- 2.1 million people (12 and older) with Opioid Use Disorder in 2017
- Crucial need to expand access to evidence-based treatments, including medication-assisted therapy (MAT)
- High rates of relapse

Naloxone – Expanded Access is Recommended

Many organizations strongly recommend that naloxone and opioid overdose education be readily accessible to individuals likely to witness a life-threatening opioid overdose (World, Federal, State, Medical)
### Take-Home Naloxone (THN)

**Considerations for Risk-Based vs Universal Prescribing**

<table>
<thead>
<tr>
<th>RISK-BASED THN</th>
<th>PROS</th>
<th>CONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reaches a defined at-risk population</td>
<td></td>
<td>Time consuming</td>
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<tr>
<td>Engages patients in conversations about risk</td>
<td></td>
<td>Complicated</td>
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<tr>
<td><strong>UNIVERSAL THN</strong></td>
<td></td>
<td>May miss patients at risk</td>
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<tr>
<td>Reaches a broader population</td>
<td></td>
<td>Increased pharmaceutical spend</td>
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<td>Less targeting/stigma</td>
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<td>More potential for rare adverse events and inappropriate administration</td>
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<td>More efficient to HCP office</td>
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PROS

- Engages patients in conversations about risk

CONS

- Time consuming
- Complicated
- May miss patients at risk

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# Opioid Overdose Risk Factors

## COMORBIDITIES

<table>
<thead>
<tr>
<th></th>
<th>Psychiatric</th>
<th>Nervous</th>
<th>Respiratory</th>
<th>Hepatobiliary</th>
<th>Renal/genitourinary</th>
<th>Gastrointestinal</th>
<th>Traumatic injury</th>
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<tbody>
<tr>
<td>VHA RIOSORD*</td>
<td></td>
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<tr>
<td>CIP RIOSORD*</td>
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## TREATMENT-RELATED

<table>
<thead>
<tr>
<th></th>
<th>ER/LA formulations</th>
<th>Benzodiazepines</th>
<th>MME/day</th>
<th>Duration of opioid therapy</th>
<th>Prior opioid overdose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIGH ≥50</td>
<td>HIGH</td>
<td>HIGH</td>
<td>HIGH</td>
<td>≥20</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>HIGH</td>
<td>HIGH</td>
<td>≥100</td>
</tr>
</tbody>
</table>

VHA = Veterans' Health Administration;  
CIP = Commercial Insured health Plan;  
RIOSORD = Risk Index for Overdose or Serious Opioid-induced Respiratory Depression;  
ER/LA = extended-release/long-acting.
Two Recent Studies Examined a Universal Precautions Approach to Overdose Education and Naloxone

• **Universal Precautions - Chronic Pain**
  Prospective, single site, n=164 (18 or older), median morphine equivalent dose of 90 med/day, overdose education and naloxone instruction provided
  – Difficulty of predicting which patients on chronic opioid therapy (COT) will experience opioid overdose
  – In previous studies, naloxone was given to only high risk patients
  – Universal Precautions (all patients receiving COT) may have significant impact on intentional and unintentional overdose deaths

• **Universal Precautions - Opioid Use Disorder**
  Prospective, single site, n=244 (18 or older) in medication assisted treatment; overdose education and naloxone instruction provided
  – There is evidence that take home naloxone can help prevent opioid overdose deaths in targeted populations
  – Participants with a diagnosis of OUD in an outpatient treatment program (OTP) setting were enrolled
  – Study suggests a model for naloxone could be replicated in other OTP settings to reduce opioid overdose deaths

Treating Chronic Conditions is Challenging
A Clinician’s Perspective

• **Chronic Pain and Opioid Use Disorder (OUD) are chronic conditions**
  – Goals of any long term chronic disease (i.e. diabetes, asthma) are to maximize benefits while managing risk of treatments and progression of disease
    • Individualized treatment for these conditions can drain resources (time, energy, finances)
    • Optimal management of these and other chronic conditions involves other individuals as well (family, friends, other caregivers)
  – Limited data on effective long-term therapies to treat Chronic Pain and OUD
  – With any chronic condition, relapse (of some degree) is expected
  – Return to function vs. symptom reduction
  – Chronic management vs. cure
Recommendations

• **Naloxone should be an integral component of treatment for patients:**
  – On chronic opioid therapy; or
  – With a diagnosis of OUD

• **Health care providers, pharmacists and patients should be educated on naloxone as a life-saving, emergency intervention for opioid overdose**

• **Access to naloxone should be increased for:**
  – People who misuse or abuse opioids, and are not in treatment (harm reduction / naloxone distribution programs)
  – Concerned family members and friends (accidental exposure, potential witness)
Omar Khalil
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