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Opioid Overdose Risk Prevention
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This newsletter is published by the New Mexico (NM) Drug Utilization Review (DUR) Board to promote safe and cost-effective drug therapy in the NM Fee-For-Service (FFS) Program. It is our hope that this educational newsletter will be useful to your practice.

According to the Centers for Disease Control and Prevention (CDC), death from opioid-related drug overdose is a significant public health burden in the U.S. More than six out of ten drug overdoses involved an opioid. During 1999 to 2014, more than 165,000 people died from overdose related to opioid pain medications. Opioid pain medication sales have increased in parallel with opioid-related overdose deaths. In 2013, it was estimated that the total health care costs of prescription opioid abuse in the U.S. was $78.5 billion per year.

In 2014, NM had the second-highest drug overdose death rate in the nation. During 2010 through 2014, the most common drugs causing unintentional overdose deaths were from prescription opioids (48%). In a 2015 analysis, it was estimated that the total health care costs of prescription opioid abuse in NM was $193 million per year.

The opioid epidemic has a disproportionate impact on Medicaid beneficiaries, who are prescribed painkillers at twice the rate of non-Medicaid patients and have three to six times the risk of overdose from prescription painkillers. The most common opioids causing unintentional overdose deaths are methadone, oxycodone, and morphine. The increased number of prescriptions, higher doses, longer course of treatment and use of opioids in conjunction with benzodiazepines are primary drivers for the overdose deaths. Identification of patients at risk of overdose, prescribing safer and more effective treatment options, adopting health-system strategies for mitigating prescription drug abuse and providing naloxone to reverse opioid overdose for high risk patients may lead to a reduction in overdose deaths and associated costs.

Identifying Patients at High Risk for Opioid Overdose Death

Patients 65 Years of Age or Older: Older patients have reduced renal function and medication clearance, increased susceptibility to accumulation of opioids and a smaller therapeutic window between safe dosages and those associated with respiratory depression and overdose. Some older adults suffer from cognitive impairment increasing risk for medication errors. Moreover, older adults have co-morbid medical conditions resulting in multiple medications including benzodiazepines which might interact with opioids.

Patients with Breathing Disorders: Careful monitoring and cautious dose titration should be used if opioids are prescribed for patients with sleep apnea or other causes of sleep-disordered breathing. Additional respiratory-related risk factors include smoking, chronic bronchitis, emphysema, asthma, respiratory infection and other respiratory illnesses.
Patients with Mental Health Conditions: Clinicians should use additional caution and increased monitoring to lessen the increased risk for opioid use disorder among patients with mental health conditions, such as depression, anxiety disorders and post-traumatic stress disorder (PTSD). Opioid therapy should not be initiated during acute psychiatric instability or uncontrolled suicide risk. Clinicians should consider behavioral health specialist consultation for patients with a history of suicide attempt or psychiatric disorder. In addition, patients with anxiety disorders and other mental health conditions are more likely to receive benzodiazepines, which can exacerbate opioid-induced respiratory depression and increase risk for overdose. Clinicians should ensure that treatment for depression and other mental health condition is optimized, consulting with behavioral health specialists when needed. Treatment for depression can also improve pain symptoms and might decrease overdose risk. For treatment of chronic pain in patients with depression, clinicians should strongly consider using SNRI antidepressants, such as venlafaxine and duloxetine, for analgesic as well as antidepressant effects if not contraindicated.2

Patients with Substance Use Disorder (SUD): Illicit drugs and alcohol are contributory factors for opioid-related overdose deaths. Clinicians should ask patients about their drug and alcohol use. Further, clinicians should use Prescription Drug Monitoring Programs (PDMPs) and drug testing to assess for concurrent substance use that increases risk for opioid use disorder and overdose. Clinicians should consider consulting SUD specialists and pain specialists regarding pain management for persons with active or recent past history of substance abuse.2

Patients with Prior Nonfatal Overdose: Prior nonfatal overdose may substantially increase risk for future nonfatal or fatal opioid overdose. If patients experience nonfatal opioid overdose, clinicians should work with them to reduce opioid dosage and to discontinue opioids when possible.

Patients Mixing Opioids with Other Drugs: Studies show that 31%–61% of fatal overdoses are related to concurrent use of opioids and benzodiazepines. Further, opioid-related deaths were more likely to occur in patients who obtained opioids from multiple physicians and pharmacies.2 In August 2016, the FDA released a warning about the concurrent use of opioids and benzodiazepines requiring manufacturers to change drug product labeling and patient information.8

CDC Guideline for Safe and Appropriate Prescribing of Opiates for Chronic Pain

In 2016, the CDC released a guideline for primary care clinicians, who prescribe opioids for chronic pain in adults. The guideline includes safe and appropriate treatment options, methods to improve patient outcomes such as reduced pain and improved function and strategies to decrease opioid use disorder, overdose and adverse events. The guideline is not intended for management of active cancer treatment, palliative care, or end-of-life care.2 Highlights of the guideline include:

- Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if benefits outweigh risks. Opioids should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate. Clinicians should establish treatment goals with patients and consider how therapy will be discontinued if there is no clinically meaningful improvement in pain and function.2

- Clinicians should prescribe immediate-release opioids instead of extended-release/long-acting opioids when starting opioid therapy for chronic pain. The lowest effective dosage
should be prescribed. Clinicians should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage ≥90 MME/day.2

- When opioids are used for acute pain, clinicians should not prescribe a greater quantity than needed. Three days or less are often sufficient; more than seven days are rarely needed. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy or dose escalation and evaluate continued therapy every 3 months or more frequently. Clinicians should optimize other therapies if possible and taper opioids to lower dosages or taper to discontinue the opioid.2

- Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors and offer naloxone in patients at high risk for overdose. Clinicians should review the PDMP data when starting opioid therapy and periodically during therapy for chronic pain. Clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible. Clinicians should offer medication-assisted treatment (MAT) with buprenorphine, methadone, or naltrexone in combination with behavioral therapies for patients with opioid use disorder.2

Naloxone for Opioid-Related Overdose

Clinicians should consider offering naloxone when prescribing opioids in patients at high risk for overdose. However, it is preferable not to initiate opioid treatment when factors that increase risk for opioid-related harms are present.2

Naloxone is an opioid-receptor antagonist that is used to reverse opioid-induced respiratory and/or central nervous system depression. Naloxone competes for the same receptor sites as opioids and reverses the opioid’s effect, such as respiratory depression, sedation and hypotension. The antagonism displayed by naloxone is competitive and short-lived, possibly necessitating repeat doses when long-acting opiates are involved.2

Naloxone is commercially available as an injection and as a nasal spray. The nasal spray (Narcan®) and auto-injector (Evzio™) are specific for use in opioid overdose outside of a medical setting. Both the nasal spray and auto-injector can be used in all age groups. Both manufacturers recommend that the nasal spray and auto-injector not be used as a substitute for emergency medical care. They also advise that family members, caregivers, or other people who may have to use naloxone in an opioid emergency should know where naloxone is stored and how to give it before an opioid emergency happens.9,10

The nasal spray (Narcan®) is administered as a single spray into one nostril. Additional doses may be administered every two to three minutes in alternating nostrils if the patient does not respond or relapses into respiratory depression. The administration should be continued until there is a response or medical assistance arrives. It is available as a single package that contains two individual bottles of the nasal spray. Each bottle contains one 4 mg dose and should not be reused.9

The naloxone auto-injector (Evzio™) uses an electronic voice instruction system to assist with administration. The auto-injector should be administered as a subcutaneous or intramuscular (IM) injection into the thigh. As with the nasal spray, the doses may be administered every two to three minutes in alternating areas of the thigh if the patient does not respond or relapses into respiratory depression. The administration should be continued until there is a response or medical assistance arrives. Evzio™ is available as a single package that contains two auto-
injectors and a training device. Each auto-injector contains one 0.4 mg dose and should not be reused.\textsuperscript{10}

Clinical trials compared the nasal administration to the IM administration of naloxone. They concluded that the nasal route achieved the same or higher levels of naloxone compared to naloxone that was administered intramuscularly. The levels were obtained in about the same amount of time for each route of administration.\textsuperscript{10} The cost of the Narcan\textsuperscript{®} nasal spray is much less expensive than Evzio\textsuperscript{™}. Thus, the nasal spray formulation is preferred in the NM Medicaid FFS program.

Naloxone Rescue Kits (NRKs) are another option for opioid overdose. The NRK requires education of assembly by a pharmacist and includes a mucosal atomization device for intranasal use or a needle for IM use. It is not FDA approved, but the average cost is less than Narcan\textsuperscript{®} nasal spray and Evzio\textsuperscript{™}.\textsuperscript{7} Due to supply problems with the atomizer; the intranasal formulation may not be readily available in NM pharmacies.

Pharmacists are authorized to dispense naloxone without a prescription in NM to a patient (or their family member) at risk for overdose to promote ease of access to naloxone. A patient consent form must be completed and signed before naloxone is prescribed and dispensed. The pharmacist must notify the patient’s primary care provider with the consent of the patient within 15 days of the original prescription. Additionally, pharmacists are required to complete a certification program approved by the NM Board of Pharmacy and maintain two hours of live continuing education in this area every two years. NM’s Medicaid FFS program reimburses pharmacies for dispensing naloxone. A claim can be submitted using the appropriate claim form.\textsuperscript{11,12}

**Centers for Medicare and Medicaid Services (CMS) Strategies for State Medicaid Programs**

In 2016, CMS released an informational bulletin on prescription opioid overdoses, misuse and addiction. The bulletin highlights emerging Medicaid pharmacy benefit management strategies for preventing opioid-related harms.\textsuperscript{6}

CMS urges that states remove methadone for pain from their preferred drug lists. This is consistent with the recommendation from the CDC that methadone should not be considered a drug of first choice by prescribers or insurers for chronic non-cancer pain.\textsuperscript{6} Although the NM FFS Medicaid program has an open formulary, prescribers are urged to comply with this CMS initiative.

Examples of CMS recommended strategies that may be used to minimize abuse and decrease opioid overdose deaths in the NM Medicaid FFS program include: establishing clinical criteria; employing step therapy with the trial of a preferred opioid; requiring prior authorization to obtain permission to prescribe certain opioids; imposing quantity limits; conducting retrospective and prospective drug utilization reviews; providing access to naloxone; and implementing lock-in programs.\textsuperscript{6}

Clinicians are encouraged to use the NM PDMP, which has been shown to be effective in preventing drug diversion when providers review a patient’s history of dispensed controlled substances. In addition, it allows states to identify patients that need addiction or pain management support. PDMPs are most effective when they are used by all clinicians.\textsuperscript{6}

Medicaid beneficiaries should have access to MAT, which uses FDA-approved medications in combination with behavioral therapies to treat SUD. Although MAT has significant evidence to support it as an effective treatment, it remains highly underused. Buprenorphine, methadone
and naltrexone are the three medications approved by the FDA for opioid dependence. Studies have shown that the most effective treatments for opioid use disorders are those that include a set of comprehensive medical, social, psychological and rehabilitation services that address all the needs of the individual.  

To report medical fraud, contact the Medicaid Quality Assurance Bureau at NM Medicaid Fraud@state.nm.us or (505) 827-3100. We appreciate your continued support of our efforts to encourage quality care for our Medicaid clients.  

Questions and/or comments about this newsletter may be directed to Diana Moya, R.Ph. at (505) 827-3174 or DianaJ.Moya@state.nm.us. DUR newsletters are posted on the New Mexico Human Services Department website: http://www.hsd.state.nm.us/providers/utilization-review.aspx.  

References:  