OPIOID USE DISORDER: MEDICATION-ASSISTED TREATMENT & LAW

CHANGES IN OKLAHOMA LAW IMPACTING PHARMACY PRACTICE AND PHARMACIST-LED NALOXONE DISTRIBUTION

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DISCLOSURES

- Under guidelines established by the Accreditation Council for Pharmacy Education, disclosure must be made regarding financial relationships with commercial interests within the last 12 months
- Sarah Johnston and Jonathan Willett have no relevant financial relationships or affiliations with commercial interests to disclose
LEARNING OBJECTIVES

At the completion of this activity, pharmacists will be able to:
1. Review recent changes to Oklahoma opioid prescription medication legislation
2. Identify potential impacts opioid legislative changes may have on tribal pharmacy practice
3. Describe implementation of a pharmacist-managed medication-assisted treatment protocol and clinic

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1. Review recent changes to Oklahoma opioid prescription medication legislation
2. Identify potential impacts opioid legislative changes may have on tribal pharmacy practice

PRE-ASSESSMENT QUESTIONS

1. Select a recent change to Oklahoma opioid prescription medication legislation:
   A. Initial prescriptions for acute pain cannot exceed a 7-day supply
   B. After a third prescription patients must enter into a patient provider agreement
   C. In 2020, Oklahoma intends to require electronic prescribing of all controlled substances
   D. Requires a discussion and documentation of risk during opioid prescribing
   E. All of the above
PRE-ASSESSMENT QUESTIONS (CONT.)

2. What is an effect that pharmacist-led naloxone distribution can have on patient outcomes?
   A. Increase a patient’s risk of opioid related death through having the product nearby
   B. Save a patient’s life in case of opioid related respiratory depression
   C. Increase the rate of overdose in rural areas
   D. Naloxone distribution has no effect on patient outcomes

OPIOID CRISIS

- Of all unintentional poisoning deaths in 2016 involving prescription drugs, illicit drugs or alcohol:
  - Opioids accounted for nearly half of these deaths in Oklahoma
OKLAHOMA’S RESPONSE TO THE OPIOID CRISIS

- Two new laws regulating opioid prescribing:
  - Senate Bill 1446
  - House Bill 2931

OKLAHOMA SENATE BILL 1446

- Approved May 2018
- SB 1446 effective as of Nov. 1, 2018
CHANGES TO THE EXISTING LAW

- Failure to check PMP grounds for disciplinary action
- Use of licensing board standards
- Licensee should obtain one hour of CE yearly in:
  - Pain management
  - Opioid use
  - Addiction

OBNDD BOARD NOTIFICATION

- Unsolicited notification to licensing boards:
  - Practitioners and pharmacists
  - CDS in quantities/frequencies inconsistent with safe practice
  - May be in a summary document
NEW DEFINITIONS

**Initial Prescription:**
- A patient who has not received the drug/equivalent in past year
- Requiring prescription for an acute event
  - If patient has had a previous prescription

**Acute Pain:**
- Practitioner expects to last a short time
- **NOT** for cancer, hospice or palliative care

**Chronic Pain:** Lasts beyond the usual course of healing process

INITIAL PRESCRIBING

**Should not exceed a 7-day supply for acute pain:**
- Lowest effective dose and immediate-release

**7 days after initial, another supply may be issued:**
- Not exceeding a 7-day supply
- After patient consultation
- Document rationale
- No undue risk

**At 3rd prescription issue patient provider agreement:**
- OR at initial if <18 years or pregnant
ENHANCED DOCUMENTATION REQUIREMENTS

- Initial prescribing: Enhanced risk discussion
- Reissuance:
  - Discussion of risk at 3rd script
  - Patient provider agreement
  - Continue risk discussion and documentation every three months
- Review course of treatment:
  - Addiction prevention
  - Attention to determining cause
  - Monitor compliance

POLICY REQUIREMENTS

- Maintain a written policy
- Document patient provider agreements
- Informed consent process with “qualifying opioid therapy patient”
  - Requiring opioid treatment more than 3 months
  - Prescribed benzodiazepines and opioids
  - Dose that exceeds 100 MME
### SUMMARY OF PRESCRIBING

<table>
<thead>
<tr>
<th></th>
<th>Day Supply</th>
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<tbody>
<tr>
<td><strong>Acute Pain</strong></td>
<td></td>
</tr>
<tr>
<td>Initial Rx</td>
<td>7-Day</td>
</tr>
<tr>
<td>Second Rx</td>
<td>7-Day</td>
</tr>
<tr>
<td>Third Rx</td>
<td>30 DS + RF (Non-CII)</td>
</tr>
<tr>
<td><strong>Chronic Pain</strong></td>
<td></td>
</tr>
<tr>
<td>Initial Rx</td>
<td>7-Day</td>
</tr>
<tr>
<td>Second Rx</td>
<td>7-Day</td>
</tr>
<tr>
<td>Third Rx</td>
<td>30 DS + RF (Non-CII)</td>
</tr>
<tr>
<td><strong>Three Month Review</strong></td>
<td>30 DS + RF (Non-CII)</td>
</tr>
</tbody>
</table>

### OKLAHOMA HOUSE BILL 2931

- Approved May 2018
- HB 2931 effective January 2020
ELECTRONIC PRESCRIBING

Electronic prescribing for all CDS
- Exceptions to be documented in MR include:
  - Extenuating circumstances
  - Physician dispensing
  - On-site administration
  - Prescription to be dispensed by a pharmacy on federal property
  - Practitioner with a waiver or extension
  - E-script cannot be issued in a timely manner

OBNDD OFFICIAL PRESCRIPTION FORMS

Where there is an exception to electronic prescribing, official OBNDD forms should be utilized for CDS:
- No fee
- Valid for 2 years
- Non-transferable
- OBNDD may revoke forms

**Not yet available**
DOSES ADMINISTERED BY A PRACTITIONER

- Dispensed without an electronic prescription
- Schedule II
  - Medically required doses administered are not to exceed 48-hour supply
- Schedule III and IV
  - Medically required doses administered are not to exceed 72-hour supply

CHICKASAW NATION DEPARTMENT OF HEALTH
APPROACH TO SENATE BILL 1446

- Changes to quick orders:
  - No default sig for chronic pain orders
- Note templates:
  - Prompt required documentation: Acute, Chronic, Follow-up
- Documentation of patient provider agreement
- Provider education
- Opioid policy
- Pharmacist-led naloxone distribution
IMPACT OF SENATE BILL 1446

Increased difficulty in continuing previous treatment with opioid medications.

Distributing naloxone to community members increases the chance that it will be available for use to save someone’s life in an unintentional overdose.

CHICKASAW NATION DEPARTMENT OF HEALTH APPROACH

- Interventions to combat the opioid crisis:
  - Prescriber education
  - Educational materials provided to patients
  - Tribal Opioid Response Grant
  - Medication-Assisted Treatment
  - Pharmacist-led naloxone distribution

Distribution of naloxone products throughout communities has increased:
- Between 1996 and 2014 152,283 rescue kits provided
- 26,463 reversals reported back

Family practice clinics – interdisciplinary approach:
- Excellent procurement rates

Department of Veterans’ Affairs education and distribution:
- Counseling well received
- Patient concerns: necessity, withdrawal precipitation, and stigma

Multiple IHS sites across the state


High risk patients identified via electronic medical record:
- Chronic opioid therapy
- Benzodiazepine
- Muscle relaxer

Patients will be assessed for the best contact method
- Encouraged to share information with family
- Encouraged to report use

Pharmacists will be encouraged to identify patients meeting criteria
PHARMACIST INTERVENTION

- Naloxone continues to be underutilized despite efforts
- Pharmacists are in a prime position to increase co-prescribing:
  - Catch patients while order processing
  - Able to best meet patient counseling needs
- Focus the conversation on Naloxone for safety:
  - Avoid triggering wording for patients (Addict, Illicit Drugs, Overdose)
  - Use comparisons to relate to patients
    - “Epinephrine Pen for allergic reaction” & “Having a fire extinguisher in case of a fire”
  - Use teach-back methods

UTILIZE PHARMACISTS IN ALL PRACTICE SETTINGS

- Emergency Department
- Outpatient
- Decentralized to Clinics
- Inpatient
- Telephone
RISK CRITERIA

<table>
<thead>
<tr>
<th>At Least One At-Risk Criterion:</th>
<th>Additional High Risk Criterion:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine Milligram Equivalent ≥50 mg</td>
<td>Multidrug opioid regimens</td>
</tr>
<tr>
<td>Concomitant benzodiazepine use</td>
<td>Long-term opioid use (&gt;3 months)</td>
</tr>
<tr>
<td>Concomitant muscle relaxer use</td>
<td>Elderly (&gt;65 years of age)</td>
</tr>
<tr>
<td>History of substance abuse</td>
<td>Comorbidities</td>
</tr>
<tr>
<td>History of overdose</td>
<td>Patients living in remote location</td>
</tr>
</tbody>
</table>

INTRANASAL NALOXONE HYDROCHLORIDE

- Current product of choice for this service
- Two doses per box
- Onset time – two minutes
- Withdrawal Symptoms
  - Pain, fast heart beat, high blood pressure, fever, sweating, stomach cramps, nausea, vomiting, diarrhea, agitation/irritability
- Storage - Room Temperature (59-77°F)
  - Protect from light
**MECHANISM OF ACTION**

- **Naloxone is essentially a pure opioid antagonist**
  - Competitive antagonist at all receptor sites
    - (mu, kappa, sigma)
  - Naloxone is almost completely devoid of agonistic effects
    - No opioid effects in the absence of an opioid

**ADVERSE REACTIONS AND SAFETY INFORMATION**

- **Contraindications:** Known hypersensitivity
- **Seek emergency medical assistance**
- **Risk of limited efficacy with partial agonists or mixed agonists**
- **Precipitation of severe opioid withdrawal:**
  - Aches, fever, sweating, runny nose, sneezing, piloerection, trembling, nervousness, irritability, nausea, vomiting, diarrhea and increased blood pressure/heart rate, muscle spasms, pain, headache, nasal dryness and xeroderma
**IDENTIFYING OPIOID OVERDOSE**

- Signs of an accidental overdose include:
  - Will not respond
  - Breathing is very slow or stopped
  - Fingertips and lips turning blue/purple, cold skin
  - Slow heartbeat or low blood pressure
  - Center of eye is very small “pinpoint pupils”
  - Choking/gurgling sounds
  - Body is limp

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**INTRANASAL NALOXONE ADMINISTRATION**

1. Check for a response
2. Give naloxone
3. Call 911
4. Care for individual
5. Consider giving naloxone again
6. Place individual in the recovery position

Administration of opiate antagonists:
- First responders have the authority to administer opiate antagonists without prescription
- First responders are covered under the Good Samaritan Act.

Prescription of opiate antagonists to family members by request:
- The provider shall give instruction on:
  - Spotting an overdose
  - Basic resuscitation techniques
  - Naloxone administration
  - Calling 911
- Family members are covered under the Good Samaritan Act.
A Pharmacist may prescribe and dispense Naloxone
- Without a protocol or prescription
- To anyone with overdose risk
- A family/friend of an at-risk person
- First responder

Intranasal Naloxone Hydrochloride
- May be less intimidating for patients

Use in emergency treatment
- Useful in the differential diagnosis

Indicated for partial or complete reversal of opioid depression
- Including Methadone & Mixed agonist-antagonist analgesics
  - Response may be incomplete > Higher dose may be required
SUMMARY

- SB1446 and HB2931 may reduce opioid related deaths long-term
- SB1446 has separated many from chronic opioid therapy
- HB2931 will further tighten restrictions in 2020
- Many sites may not meet electronic prescribing requirements
- Pharmacist-led naloxone distribution remains a relevant tool in combating opioid related deaths

POST-ASSESSMENT QUESTIONS

1. Select a recent change to Oklahoma opioid prescription medication legislation.
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REFERENCES

12. 63 OK Stat § 63-1-2506.2 (2014)
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Opioid Use Disorder: Medication Assisted Treatment

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June 29, 2019

Disclosure

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Learning Objectives

• At the completion of this activity, pharmacists will be able to:
  • Recognize pharmacology of buprenorphine/naloxone and why we utilize it.
  • Identify four stages of medication-assisted treatment.
  • Describe implementation of a pharmacist-managed medication-assisted treatment protocol and clinic.
• At the completion of this activity, pharmacy technicians will be able to:
  • Identify four stages of medication-assisted treatment.

Pre-Assessment Questions

What are the benefits of using buprenorphine/naloxone for medication-assisted treatment?
A. Ceiling effect
B. High affinity for opioid receptors
C. Diversion deterrent included
D. All of the above
Pre-Assessment Questions

Which phase of treatment lasts the longest?
A. Induction  
B. Stabilization  
C. Maintenance  
D. Taper

Buprenorphine/Naloxone

• Buprenorphine  
  • Mu-opioid receptor partial agonist  
  • Ceiling effect – no more benefit past a certain dose  
  • High affinity for opioid receptors  
    • Will precipitate withdrawal if other opioids are present
Buprenorphine/Naloxone

- Naloxone
  - Mu-opioid receptor antagonist
  - Poor oral bioavailability
  - Diversion deterrent

<table>
<thead>
<tr>
<th></th>
<th>Buprenorphine</th>
<th>Naloxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tmax, sublingual film</td>
<td>1.53 – 1.72 hours</td>
<td>0.77 – 0.81 hours</td>
</tr>
<tr>
<td>Bioavailability, sublingual tablet</td>
<td>15%</td>
<td>3%</td>
</tr>
<tr>
<td>*Increased with film</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolism</td>
<td>Hepatic, 2D6 and 3A4 inhibitor</td>
<td>Hepatic</td>
</tr>
<tr>
<td>Half-life</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buccal film</td>
<td>16.4 – 27.5 hours</td>
<td>1.9 – 2.4 hours</td>
</tr>
<tr>
<td>Sublingual film</td>
<td>24 – 42 hours</td>
<td>2 – 12 hours</td>
</tr>
<tr>
<td>Hepatic impairment, moderate</td>
<td>35% increase</td>
<td>165% increase</td>
</tr>
<tr>
<td>Hepatic impairment, severe</td>
<td>57% increase</td>
<td>122% increase</td>
</tr>
</tbody>
</table>
Buprenorphine/Naloxone

- Available dosage forms

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Dosage Form</th>
<th>Doses Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suboxone®</td>
<td>Sublingual strip</td>
<td>2mg/0.5mg, 4mg/1mg, 8mg/2mg, 12mg/3mg</td>
</tr>
<tr>
<td>Zubsolv®</td>
<td>Sublingual tablet</td>
<td>0.7mg/0.18mg, 1.4mg/0.36mg, 2.9mg/0.71mg, 5.7mg/1.4mg, 8.6mg/2.1mg, 11.4mg/2.9mg</td>
</tr>
<tr>
<td>Bunavail®</td>
<td>Buccal strip</td>
<td>2.1mg/0.3mg, 4.2mg/0.7mg, 6.3mg/1mg</td>
</tr>
<tr>
<td>Buprenorphine/naloxone (generic)</td>
<td>Sublingual tablet</td>
<td>2mg/0.5mg, 8mg/2mg</td>
</tr>
</tbody>
</table>
Buprenorphine/Naloxone

• Counseling points
  • May take 5 to 10 minutes to dissolve
  • Dissolves faster/easier if mouth is moist
  • Needs to dissolve completely before drinking
  • Avoid caffeine and smoking 15 to 30 minutes before dose

Buprenorphine/Naloxone

• Side Effects
  • Withdrawal symptoms
  • Constipation
  • Headache
  • Nausea/vomiting
  • Anxiety
Buprenorphine/Naloxone

*Important drug interactions*

<table>
<thead>
<tr>
<th>Classification</th>
<th>Examples</th>
<th>Potential Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td>Diazepam, alprazolam, lorazepam, etc.</td>
<td>CNS depression, respiratory depression, death</td>
</tr>
<tr>
<td>Anti-viral</td>
<td>Atazanavir</td>
<td>Decrease serum concentration of atazanavir</td>
</tr>
<tr>
<td>CYP3A4 Inducers</td>
<td>Carbamazepine, phenytoin, phenobarbital, rifampin, primidone</td>
<td>Increased metabolism of buprenorphine</td>
</tr>
</tbody>
</table>

Buprenorphine/Naloxone

<table>
<thead>
<tr>
<th>Dosing Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Impairment</td>
</tr>
<tr>
<td>Moderate Hepatic Impairment</td>
</tr>
<tr>
<td>Severe Hepatic Impairment</td>
</tr>
</tbody>
</table>
Buprenorphine/Naloxone

• Regulations
  • C-III
  • Provider must obtain DATA 2000 waiver
    • 8-hour training for MD and DO
    • 24-hour training for NP and PA
    • DEA will issue new number with “X”
    • All providers can see 30 patients during 1st year
    • Can apply to increase to 100 after 1st year

Medication-Assisted Treatment

• Four main stages:
  - Induction
  - Stabilization
  - Maintenance
  - Taper
Induction

• Patient must be in active withdrawal
• Patient must abstain from opioids for 1 to 7 days before induction can begin
  • Short-acting opioids usually 24 hours to withdrawal symptoms
  • Long-acting opioids can take up to 5 to 7 days to show withdrawal symptoms
• Clinical Opiate Withdrawal Scale (COWS)
Induction

- Patient is started on buprenorphine/naloxone and tapered over several days
- Patient may begin other withdrawal symptom medications as needed
  - Acetaminophen
  - Nausea medications
- Follow-up scheduled every 1 to 3 days
- Mental Health and Social Services initiated, based on patient need
- Patients advised to abstain from all substances

Stabilization

- Patient further titrated to personalized dose over 2 to 3 weeks
- Follow-up scheduled every 1 to 2 weeks
- Withdrawal symptoms medications may be continued if needed
- Drug screens may be performed at each visit
- Mental health services continued
- Patients advised to abstain from all substances
Maintenance

• Patient will continue on dose that was established during Stabilization
• Follow-up scheduled every 2 to 4 weeks
• Drug screens may be performed at each visit
• Longest period of treatment, will last approximately 6 to 9 months
• Mental health services will be continued
• Patients advised to abstain from all substances

Taper

• Taper will begin when patient and treatment team agree patient is ready
• Slow taper, decrease by 2mg/0.5mg from previous total daily dose per time period
• Decrease dose every 2 to 4 weeks, at scheduled follow-up appointments
• Mental health services will be continued
• Patients advised to abstain from all substances
Lab Considerations

• Urine Drug Screen
  • Specific for buprenorphine/norbuprenorphine
  • Positive screen results require further testing for verification
    • Gas Chromatography-Mass Spectrometry (GC-MS)

Mental Health Services

• Integral to treatment
  • Psychoeducation
  • Supportive Therapy
  • Motivational Therapy
  • Psychotherapy
  • Support Groups
Mental Health Services

- Patient specific plan should be developed
- Treatment should be adjusted to patient needs throughout treatment
- Goal is to treat the **WHOLE** patient

Post-Assessment Questions

What are the benefits of using buprenorphine/naloxone for medication-assisted treatment?

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B. High affinity for opioid receptors  
C. Diversion deterrent included  
D. All of the above
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Which phase of treatment lasts the longest?
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C. Maintenance
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References

1. Lexicomp
2. Suboxone® medication guide
5. National Alliance of Advocates for Buprenorphine Treatment. www.naabt.org