We Hear That!

On November 8, 2017, Katie Trambly, PharmD, Hastings, and her husband, Casey, welcomed new daughter, Evelyn. Evelyn joins her older sister, Brooklyn. Congratulations to the Trambly family!

• Congratulations to the Nebraska Medicine Specialty Pharmacy for attaining URAC reaccreditation for the next 3 years. According to NPA member Randy Moore, PharmD, the specialty pharmacy program at Nebraska Medicine was launched in 2013 and first achieved URAC 2.0 accreditation in January 2014. Nebraska Medicine Specialty Pharmacy is one of only four specialty pharmacies in Nebraska to achieve URAC accreditation. Nebraska Medicine Specialty Pharmacy program is a partnership with Nebraska Medicine Provider Offices and the Nebraska Medicine Ambulatory Pharmacy Team.

• Mark your calendar for Friday, May 25, 2018 for the 15th Annual Immunize Nebraska Conference at the Mike and Josie Harper Center, Creighton University Campus, Omaha, Nebraska. https://healthsciences.creighton.edu/events/15th-annual-immunize-nebraska

• Plan to attend the Nebraska Antimicrobial Stewardship Summit on Friday, June 1, 2018 at the Embassy Suites Omaha-La Vista Hotel & Conference Center, La Vista, Nebraska. https://unmc.edu/cce/

• This issue marks the 81st birthday for the Nebraska Mortar & Pestle (M&P). In 1937, the M&P began with a 4-page sheet layout. Please send pharmacy news for the “We Hear That” section of the M&P. You may think your news isn’t important, but M&P subscribers enjoy reading about their pharmacy friends from across the state. Send your news and photos to diane@npharm.org.

Member Emails
Are you receiving NPA emails? The NPA frequently sends emails regarding pharmacy issues and association events. Stay "in the know!" Send email changes to info@npharm.org.

Publisher
The Nebraska Mortar & Pestle (M&P) (ISSN 0028-1891) is owned and published by the Nebraska Pharmacists Association to provide continuing pharmacy education, drug information, news, and trends in the profession of pharmacy. Opinions expressed by the contributors, whether signed or otherwise, do not necessarily reflect the attitudes of the publisher nor are they responsible for them.

The M&P is published six times a year - February, April, June, August, October and December. The subscription rate for non-members is $30 per year. The managing editor is Joni Cover. The office of publication is 6221 S 58th St, Suite A, Lincoln, NE 68516-3687. Second class postage paid at Lincoln, Nebraska, and at additional mailing offices. Postmaster: send address changes to Nebraska Mortar & Pestle, 6221 S 58th St, Suite A, Lincoln, NE 68516-3687 or email m&p@npharm.org.

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In Case You Missed It

Your NPA member benefits include a daily email with important drug and health information, as well as answers to member questions. Below is a partial list of some of the most recent Daily News Dose items and other important pharmacy news that you may have missed.

Who Should Have Access to the Pharmacy?
Title 21 Code of Federal Regulations §1301.72 Physical security controls for non-practitioners:... storage areas... (d) Accessibility to storage areas. The controlled substances storage areas shall be accessible only to an absolute minimum number of specifically authorized employees. When it is necessary for employee maintenance personnel, nonemployee maintenance personnel, business guests, or visitors to be present in or pass through controlled substances storage areas, the registrant shall provide for adequate observation of the area by an employee specifically authorized in writing.

Help Sickle Cell Disease Patients be Healthy
Common illnesses, like the flu, can quickly become dangerous for a person with sickle cell disease. The best defense is to take simple steps to help prevent infections.

Pharmacists can help patients with sickle cell disease be healthy by reminding them to stay current with immunizations, and to understand the importance of hand washing to prevent illnesses and food safety to prevent salmonella infections. See CDC 5 Tips to Prevent Infection at https://www.cdc.gov/ncbddd/sicklecell/documents/tipsheets_5.pdf.

Safe Injection Champion
The Nebraska Department of Health and Human Services has a goal to recruit and train Safe Injection Champions at every location in Nebraska where injections and IV infusions are administered.

A Safe Injection Champion will have the following responsibilities:
• Stay updated on the latest safe injection practices by successfully completing one of the “Safe Injection Champion” courses
• Audit the injection practices in their facility
• Spread new information insuring the competency of the healthcare workers in their place of employment.

Learn more about the program at http://dhhs.ne.gov/publichealth/HAI/Pages/SafeInjection.aspx

Technician Certification
Pharmacy technicians MUST maintain their certification as well as their registration with the State of Nebraska.

Certified pharmacy technicians need to know the requirements for renewing their certification. Certified technician programs require continuing education hours to maintain certification and typically charge a fee for re-certification. Some require continuing education hours specifically in patient safety and law.

The NPA offers free continuing education accredited specifically for pharmacy technicians members in the Nebraska Mortar & Pestle and at the Annual Convention. If a pharmacy technician does not know their re-certification requirements, contact the program where the certification was provided.

The Pharmacist-In-Charge is responsible for making sure that all pharmacy technicians are registered with the State and their certification is current.

Drug Take Back Day
The National Prescription Drug Take Back Day aims to provide a safe, convenient, and responsible means of disposing of prescription drugs, while also educating the general public about the potential for abuse of medications, as does the Nebraska MEDS Drug Disposal program.

Remind your patients that there’s no need to wait for a DEA take back event because Everyday is a Take-Back Day in Nebraska. The Super Saver Pharmacy at 5460 S 56th Street in Lincoln is the newest pharmacy to join the program. Participating pharmacies can be found at leftovermeds.com. For more information, contact Hallie Schimenti at hallie@npharm.org or 402-420-1500.
February 9, 2018

Jerome Wohleb, PharmD, MBA, FASHP, FAzPA
Chair, Nebraska Pharmacists Association Hospital Health-System Network
6221 S 58th Street, Suite A
Lincoln, Nebraska 68516

Dear Dr. Wohleb:

I am pleased to inform you that the ASHP Board of Directors, at its January 18, 2018, meeting took the following action:

“To grant the Nebraska Pharmacists Association Hospital Health-System Network full affiliation status with ASHP in accordance with ASHP’s governing documents and the ASHP Guidelines for Affiliation with State Organizations.”

The Commission on Affiliate Relations reviewed the petition for ongoing affiliation and determined that the petition successfully addressed all requirements for ongoing affiliation based on the ASHP Guidelines for Affiliation with State Organizations. The Nebraska Pharmacists Association Hospital Health-System Network was found to be an organization that continues to reflect a mission, vision, and membership focus that is consistent and congruent with the purposes and mission of ASHP. Therefore, the Board of Directors voted to grant full affiliation status with ASHP.

On behalf of the ASHP Board of Directors, I congratulate the Nebraska Pharmacists Association Hospital Health-System Network in achieving full affiliate status through ongoing affiliate review. I look forward to a continued synergistic partnership between ASHP and the Nebraska Pharmacists Association Hospital Health-System Network in the future.

Sincerely,

Paul W. Abramowitz

cc: Joni Cover, Chief Executive Officer
Dr. Fletcher to step down as dean of College of Pharmacy

After serving as dean of the UNMC College of Pharmacy for more than a decade, Courtney Fletcher, Pharm.D., has announced that he has decided to step down effective July 1. He will remain on the college’s faculty as a professor and will continue his research and teaching endeavors.

“It has truly been an amazing decade for the College of Pharmacy,” said UNMC Chancellor Jeffrey P. Gold, M.D. “We can’t thank Dr. Fletcher enough for his outstanding leadership. He has elevated the college to an elite level, and we couldn’t be more proud of what they’ve accomplished.”

The crowning achievement during Dr. Fletcher’s deanship came in 2016 when the College of Pharmacy opened the new UNMC Center for Drug Discovery - Lozier Center for Pharmacy Sciences and Education, a $35 million building entirely constructed through private giving.

Ruth Scott, who along with her husband, Bill, was one of the two major donors for the UNMC Center for Drug Discovery - Lozier Center for Pharmacy Sciences and Education, praised Dr. Fletcher for his work as dean.

“Bill and I think the world of Courtney,” Ruth Scott said. “It was his strong leadership that gave us confidence to invest in the new building. We are thrilled that he will be staying on the faculty of the College of Pharmacy and know he will accomplish great things in his research for years to come.”

“Serving as dean has been a highlight of my professional career,” Dr. Fletcher said. “The students, staff and faculty of the College of Pharmacy are outstanding folks, and the long list of accomplishments and cultural and physical transformation that has happened over these 10 years, is remarkable and is their achievement.

“My 10 years as dean have been challenging and rewarding - and enough. This is simply the right time for me to step aside, and for the College of Pharmacy and UNMC to recruit new leadership. I’ll look forward to continuing contributions as a professor in the UNMC College of Pharmacy.”

An outstanding researcher, Dr. Fletcher received a $3.73 million, five-year grant to continue his longtime research into finding more effective drugs to wipe out HIV. In addition, he noted that he just submitted two other grant applications earlier this month.

Dr. Fletcher, 62, earned his bachelor of science degree in pharmacy (with honors) from the University of Wyoming in 1978 and his doctor of pharmacy degree from the University of Minnesota in 1982. In 2016, Dr. Fletcher was honored by the University of Wyoming School of Pharmacy as a distinguished alumnus.

Dr. Fletcher’s term as dean began in November 2007.

Distinguished Scientists and New Investigator

A ceremony to recognize outstanding researchers at UNMC was held in February. Four Pharmaceutical Sciences faculty members were honored.

Corey Hopkins, Ph.D., Associate Professor, and Joseph Vetro, Ph.D., Associate Professor, received the Distinguished Scientist Award.

The Distinguished Scientist Award -- which is sponsored by the chancellor -- recognizes researchers who have been among the most productive scientists in the country during the past five years.

The goal of Dr. Hopkins’s research is to develop new molecules that help to better understand the underlying mechanisms of disease and then translate those discoveries into new medicines.

Dr. Vetro’s research focuses on drug delivery to greatly improve cancer treatments and vaccines through the development of nanoscale-sized dosage forms that increase the localization of conventional and unconventional drugs to their sites of action in the body.

Aaron Mohs, Assistant Professor, received the New Investigator award. The goal of Dr. Mohs’s research is to develop imaging agents that can be used for multiple applications, including helping to detect and guide removal of cancerous lesions, learning more about cancer biology, and finding ways to better detect and identify pathogenic microorganism.

New Investigator Awards go to outstanding UNMC scientists who in the past two years have secured their first funding from the National Institutes of Health, the Department of Defense or other national sources. New Investigators also had to demonstrate scholarly activity such as publishing their research and/or presenting their findings at national conventions.

Dr. Sam Sanderson was recognized posthumously as a distinguished scientist for his research on an immune stimulating peptide called EP67. Dr. Sanderson worked 27 years at the medical center, most recently as research associate professor in the UNMC College of Pharmacy, and founded the startup company, Prommune, Inc., in 2002, based on his research. Sam’s family was there to accept the award.
Objectives

At the conclusion of this lesson, pharmacists and pharmacy technicians should be able to:

1. Identify the prevalence and mechanism of opioid induced constipation (OIC).
2. Describe the clinical guidance for management of OIC.
3. State the dosing, administration, and adverse effects for methylnaltrexone, naloxegol, naldemedine, and lubiprostone.

Background

Opioid use in the United States has significantly increased over the years. Americans consume approximately 80 percent of the global supply of opioids, although the United States represents only five percent of the global population. It is estimated that 300 million opioid pain prescriptions were written in the United States in 2015 alone.\(^1\)

Opioids are the most commonly prescribed class of medication for chronic non-cancer pain, and while effective in alleviating severe pain, they can cause adverse effects including opioid induced constipation (OIC).\(^2\) Studies estimate that 40 to 50 percent of patients with non-cancer pain experience OIC.\(^3\) OIC can negatively impact a patient’s quality of life, as well as productivity and activity levels. It can lead to missed work days and impaired job-related performance. OIC may also interfere with the ability of opioids to control pain; patients may stop or decrease opioid therapy to obtain relief from OIC, which may undermine the clinical benefit.\(^3\) Therefore, it is important to treat patients who are experiencing OIC.

This CPE lesson was written by the following from the Creighton University School of Pharmacy & Health Professions: Tiffany Ramos, PharmD, PGY1 Pharmacy Practice Resident; Karen O’Brien, PharmD, Associate Professor; Shana Castillo, PharmD, MBA, Assistant Professor; Eric Hoie, PharmD, Associate Professor; and Kimberley Begley, PharmD, Associate Professor; none of whom do not have any conflicts of interest nor any financial relationships with a commercial interest related to this activity.
Mechanism of OIC
The action of opioids is mediated through Mu(µ), Delta (δ), and Kappa (K) opioid receptors which are distributed throughout the central, peripheral, and enteric nervous systems. The µ-opioid receptor is the primary receptor through which opioid analgesics function. The high density of µ receptors in the enteric system appears to cause most of the gastrointestinal (GI) adverse effects which include constipation, nausea, vomiting, abdominal cramping, bloating and abdominal pain. In the GI tract, opioids facilitate several effects that lead to constipation. Peristaltic movement is decreased, resulting in increased transit time through the gut. Absorption of fluids from the GI tract is increased and intestinal secretions are decreased, leading to hard, dry stools. Further, opioids increase anal sphincter muscle tone and decrease reflex relaxation, contributing to difficulty in rectal evacuation.

Tolerance to the µ-opioid effects does not occur in the colon, although it does in other GI organs. Therefore, patients using opioids long-term develop a tolerance to GI side effects, except for constipation. Opioid tolerance develops through the downregulation of an intracellular protein, β-arrestin-2, in the ileum; however, β-arrestin-2 expression is preserved in the colon. Several prescription medications targeting the underlying pathophysiology of OIC have been approved by the Food and Drug Administration (FDA).

Diagnosis
There is no current consensus for the definition of OIC. The American College of Gastroenterology defines constipation as “unsatisfactory defecation with infrequent bowel movements and/or difficult stool passage”. The Rome diagnostic criteria, an influential standard in defining functional GI disorders, was recently updated to include diagnostic criteria for OIC (Table 1), yet barriers to properly diagnose OIC still exist. There may be a lack of awareness among clinicians about OIC and patients might be ashamed to disclose their symptoms to clinicians. This could lead to the underdiagnosis of OIC and prevent patients from receiving appropriate treatment.

Clinical Guidance
There are no current treatment guidelines for OIC, but there is clinical guidance for its management. The first step is nonpharmacologic lifestyle modifications. These should be employed at the initiation of opioid therapy and continued for the duration of treatment. This includes increasing consumption of dietary fiber, oral fluids, and physical activity. If nonpharmacologic measures are insufficient alone, nonprescription pharmacologic options may be pursued. Nonprescription medications appropriate for OIC include stimulants, stool softeners, bulk-forming laxatives, and enemas. Nonprescription laxatives do not treat the underlying mechanism of OIC and may not provide adequate symptom relief for all patients. Thus, there is inadequate evidence to support their use in the management of OIC. If treatment with nonprescription products is unsuccessful, prescription medications approved for the treatment of OIC may be considered.

OIC Treatment
Two classes of prescription medications have recently been approved for the treatment of OIC, chloride channel activators and peripherally-acting mu-opioid receptor antagonists (PAMORAs). Only PAMORAs target the specific underlying cause of OIC - the binding of opioids to the µ receptors in the enteric nervous system. PAMORAs work by selectively inhibiting opioid receptors in the gut, thus decreasing the constipating effect of opioids while still maintaining the analgesic effects. There are currently four approved drugs for the treatment of OIC (Table 2). Lubiprostone (Amitiza) is the only chloride channel activator approved for OIC. Methylnaltrexone (Relistor), naloxegol (Movantik), and naldemedine (Symproic) are the PAMORAs on the market approved for OIC.

Methylnaltrexone (Relistor)
Methylnaltrexone injections were approved by the FDA in 2008, with the tablets gaining FDA approval in 2016. Methylnaltrexone is a PAMORA that reduces orocecal transit time, which is the time required for intestinal contents to pass through the intestinal tract, without affecting analgesia or causing opioid withdrawal. Both formulations are FDA approved for the treatment of OIC in adults with chronic non-cancer pain. Methylnaltrexone injection is also indicated for the treatment of...
### Table 2 | FDA Approved Drugs for OIC

<table>
<thead>
<tr>
<th>Drug (Brand)</th>
<th>Dosing for OIC in adult patients with chronic non-cancer pain</th>
<th>Hepatic Impairment Dosing</th>
<th>Renal Impairment Dosing (CrCl &lt; 60 mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methylnaltrexone</strong> (Relistor)</td>
<td>Tablets 450 mg orally once daily in the morning</td>
<td>Child Pugh A&lt;br&gt;Tablets No adjustment&lt;br&gt;Injections No adjustment</td>
<td>Tablets 150 mg orally once daily</td>
</tr>
<tr>
<td></td>
<td>Injections 12 mg subcutaneously once daily</td>
<td>Child Pugh B&lt;br&gt;Tablets 150 mg orally once daily&lt;br&gt;Injections No adjustment</td>
<td>Injections 6 mg subcutaneously once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Child Pugh C&lt;br&gt;Tablets 150 mg orally once daily&lt;br&gt;Injections Not studied</td>
<td></td>
</tr>
<tr>
<td><strong>Naloxegol</strong> (Movantik)</td>
<td>25 mg orally once daily, can be decreased to 12.5 mg orally once daily if not tolerated</td>
<td>Child Pugh A and B&lt;br&gt;No adjustment</td>
<td>12.5 mg orally once daily, can be increased to 25 mg orally once daily if tolerated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Child Pugh C&lt;br&gt;Avoid use</td>
<td></td>
</tr>
<tr>
<td><strong>Naldemedine</strong> (Symproic)</td>
<td>0.2 mg orally once daily with or without food</td>
<td>Child Pugh A and B&lt;br&gt;No adjustment</td>
<td>Specific guidelines are not available but it appears that no dosage adjustment is necessary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Child Pugh C&lt;br&gt;Avoid use</td>
<td></td>
</tr>
<tr>
<td><strong>Lubiprostone</strong> (Amitiza)</td>
<td>24 mcg orally twice daily</td>
<td>Child Pugh A&lt;br&gt;No adjustment</td>
<td>No adjustment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Child Pugh B&lt;br&gt;16 mcg orally twice daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Child Pugh C&lt;br&gt;8 mcg orally twice daily</td>
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OIC in adults with advanced illness who are receiving palliative care when response to laxatives has not been sufficient. Methylnaltrexone is available as 150 mg tablets, as well as 8 mg/0.4 mL and 12 mg/0.6 mL single-dose prefilled syringes. It is also available as a 12 mg/0.6 mL single-dose vial. The recommended adult dose for OIC in patients with chronic non-cancer pain is 450 mg orally once daily in the morning or 12 mg subcutaneously once daily (Table 2). No dose reduction is necessary for the oral or injectable formulation in patients with mild hepatic impairment (Child-Pugh Class A). In patients with moderate to severe hepatic impairment (Child-Pugh Class B or C), the oral dose should be reduced to 150 mg orally once daily. No dose reduction is necessary for the injectable formulation in patients with moderate hepatic impairment (Child-Pugh Class B) and the injectable formulation was not studied in patients with severe hepatic impairment (Child-Pugh Class C). The Child Pugh score is based on total bilirubin, serum albumin, ascites, hepatic encephalopathy, and international normalized ratio (INR). In patients with a CrCl < 60 mL/min, the oral dose should be reduced to 6 mg subcutaneously once daily. Both formulations are well tolerated and the most common adverse effects in patients with chronic non-cancer pain are abdominal pain, nausea, diarrhea, hyperhidrosis, and chills. Methylnaltrexone has a drug interaction with opioid antagonists resulting in potential increased risk of opioid withdrawal. Use of methylnaltrexone in patients with known or suspected mechanical GI obstruction and at an increased risk of recurrent obstruction is contraindicated because of the potential risk of GI perforation.
Patients should be instructed to take the oral methylnaltrexone tablets at least 30 minutes before the first meal of the day. With the injectable formulation, counseling should include a review of proper injection technique and disposal if self-injecting. Injections should be administered subcutaneously into either the upper arm, abdomen, or thigh. Patients administering self-injections should not inject into the upper arm. Injection sites should be rotated, avoiding areas with scars or stretch marks. The single use vial should be immediately discarded once the dose is drawn up since no preservatives are present. Prefilled syringes need to be protected from light and should only be removed from their tray when the patient is ready to administer the dose. Patients should be near a bathroom when administering the medication as they may experience an immediate effect.9

**Naloxegol (Movantik)**

Naloxegol was approved in 2014 and is indicated for the treatment of OIC in patients with chronic non-cancer pain. Naloxegol is a PAMORA with a similar mechanism of action to methylnaltrexone. It is available as 12.5 mg and 25 mg tablets.11 The recommended adult dose for OIC is 25 mg once daily in the morning on an empty stomach. If this dose is not tolerated, it may be reduced to 12.5 mg once daily (Table 2). In patients with mild to moderate hepatic impairment (Child-Pugh Class A or B), a dose reduction is not necessary, but use should be avoided in patients with severe hepatic impairment (Child-Pugh Class C). In patients with a CrCl < 60 mL/min, the initial dose should be 12.5 mg once daily. If the dose is tolerated, but OIC symptoms persist, it may be increased to 25 mg once daily.12 Naloxegol is well tolerated and the most common adverse effects are abdominal pain, diarrhea, nausea, headache, flatulence, and vomiting.10 Naloxegol is primarily metabolized by CYP3A4, and therefore has drug interactions with moderate to strong 3A4 inhibitors and strong 3A4 inducers. Naloxegol should not be used with other opioid antagonists as concomitant use may increase the risk of opioid withdrawal. Naloxegol is contraindicated in patients with known or suspected GI obstruction or at increased risk of recurrent obstruction, as well as in patients using strong 3A4 inhibitors concomitantly.13

Patients should discontinue all maintenance laxatives prior to initiating naloxegol. Laxatives may be used if there is a suboptimal response to therapy after three days. Naloxegol should be taken on an empty stomach at least one hour prior to the first meal or two hours after the meal. Co-administration with grapefruit and grapefruit juice should be avoided. Patients unable to swallow the tablet whole can crush the tablet into a powder, mix with four fluid ounces of water, and drink immediately. The glass should then be refilled with another four fluid ounces of water, stirred and the contents drunk.12

**Naldemedine (Symproic)**

Naldemedine is a PAMORA that was approved in March 2017 for the treatment of OIC in adult patients with chronic non-cancer pain.14 Naldemedine is a derivative of naltrexone; however, it has an additional side chain which decreases its ability to penetrate the blood brain barrier.13,14 Naldemedine is available as 0.2 mg tablets and the recommended dose for adults is 0.2 mg by mouth once a day.15 (Table 2) There is no dosage adjustment required for patients with mild to moderate hepatic impairment; however, use should be avoided in patients with severe hepatic impairment. Guidelines for use in renal impairment have not been established, but it appears a dosage adjustment is not necessary.14 The most common adverse effects reported with naldemedine use are abdominal pain, diarrhea, nausea, and gastroenteritis.13 Metabolism of naldemedine occurs mainly via CYP3A4; therefore, use with strong CYP3A inducers should be avoided due to anticipated decreased concentrations of naldemedine. If using with a moderate or strong CYP3A4 inhibitor or P-glycoprotein inhibitor, increased concentrations of naldemedine can be expected and the patient should be monitored for adverse reactions.13 Use with other opioid antagonists should be avoided due to the potential for additive effects and opioid withdrawal.13 Due to the possibility of gastrointestinal perforation, naldemedine is contraindicated in patients who have a known or suspected gastrointestinal obstruction and in patients who have an increased risk of recurrent obstruction.13,14

Naldemedine may be taken with or without food. Patients should be instructed to discontinue naldemedine if they discontinue their opioid analgesics.13,14

**Lubiprostone (Amitiza)**

Lubiprostone was approved in 2006 for the treatment of chronic idiopathic constipation in adults and treatment of irritable bowel syndrome with constipation in women at least 18 years old in 2008. In 2013, it gained additional approval to treat OIC in patients with chronic non-cancer pain.16 Lubiprostone is a chloride channel activator that increases intestinal fluid secretion which softens the stool, increases motility in the intestine, and promotes spontaneous bowel movements.16 It is available as 8 mcg and 24 mcg capsules. The recommended adult dose for OIC is 24 mcg twice daily with food and water (Table 2). In patients with moderate hepatic impairment (Child-Pugh Class B), the dose should be reduced to 16 mcg twice daily and to 8 mcg twice daily in patients with severe hepatic impairment (Child-Pugh Class C). No dose adjustment is necessary in patients with mild hepatic impairment (Child-Pugh Class A) or renal impairment.16 Lubiprostone is well tolerated and the most common adverse effects are nausea and diarrhea.15 A drug-drug interaction may occur with diphenylheptane opioids,
such as methadone, which can dose dependently reduce lubiprostone’s activation of chloride channels in the GI tract. Lubiprostone is contraindicated in patients with known or suspected mechanical GI obstruction.15

Patients should swallow lubiprostone capsules whole. Administering lubiprostone with food minimizes the symptoms of drug induced nausea.16

Pharmacist’s Role
Pharmacists can play an important role in helping patients manage OIC by educating them about treatment options and acting as a patient advocate. When patients receive a new opioid prescription, pharmacists should counsel about the possibility of OIC, even at low doses. Pharmacists should suggest lifestyle modifications such as increasing exercise and consuming a high fiber diet, while patients are taking opioids to prevent OIC.

Patients may be reluctant to discuss constipation issues with their physician, fear that the physician will reduce the dose of their opioid medication, or simply not realize constipation can result from taking opioids. As the last health care provider to interact with a patient before an opioid medication is dispensed, pharmacists have the final opportunity to provide education about OIC and discuss treatment options. If patients have tried multiple OTC laxatives, the pharmacist can recommend the patient discuss prescription alternatives with their physician. Patients may not be aware that there are prescription medications available to manage OIC.

Conclusion
OIC is the most common adverse effect of opioids. OIC can occur in any patient who is taking any opioid at any dose. Several prescription medications have been approved for the management of OIC. These medications can provide relief in patients who have not experienced relief from lifestyle modifications and nonprescription medications. OIC can severely impair a patient’s quality of life and pharmacists can positively impact outcomes by educating patients about OIC and discussing both nonprescription and prescription medications which may help relieve symptoms.

References

Quiz answers may be submitted:
Online: www.npharm.org
Fax: 402-420-1406
Email: m&p@npharm.org
Mail: Nebraska Mortar & Pestle
6221 S 58th St, Ste A
Lincoln, NE 68516

The Nebraska Pharmacists Association disclaims any liability to you or your patients resulting from reliance solely upon the information contained herein.

Policies for the Nebraska Mortar & Pestle (M&P) continuing pharmacy education lessons and quizzes:
1. M&P Quizzes are valid only for the membership year in which they are published. Quizzes for the 2018 Membership Year must be received by December 12, 2018. Quizzes cannot be carried over to another membership year.
2. If more than three questions are missed, the quiz will be returned. The quiz can be resubmitted.
3. CPE transcripts can be printed from NABP e-Profiles at www.nabp.net.
4. CPE credits are submitted to NABP by the 15th of each month. For example, M&P CPE quizzes completed in the month of June 2018 will be sent to NABP e-Profiles before July 15, 2018.
Management of Opioid Induced Constipation

Quiz #4, April 2018, ACPE 0128-0000-18-017-H01-P/T

1. ____ of patients with non-cancer pain are estimated to experience OIC.
   a. 10 to 20%
   b. 25 to 35%
   c. 40 to 50%
   d. 55 to 65%

2. Opioids commonly facilitate ____ which leads to constipation.
   a. decreased transit time through the gut.
   b. decreased anal sphincter muscle tone.
   c. increased absorption of fluids from the GI tract.
   d. increased intestinal secretions.

3. The first step in the management of OIC is the use of ____.
   a. chloride channel activators
   b. nonpharmacologic lifestyle modifications
   c. nonprescription pharmacologic options
   d. peripherally-acting mu-opioid receptor antagonists

4. What is the mechanism of action of the PAMORAs?
   a. Activate chloride channels in the gut.
   b. Bind opioid receptors in the gut.
   c. Increase fluid secretion in the gut.
   d. Selectively inhibit the opioid receptor in the gut.

5. The mechanism of action of lubiprostone is to ____.
   a. activate chloride channels in the gut
   b. bind opioid receptors in the gut
   c. increase fluid secretion in the gut
   d. selectively inhibit the opioid receptor in the gut

6. ____ are the most common adverse effects of methylnaltrexone in patients with chronic pain.
   a. Abdominal pain, nausea, diarrhea, hyperhidrosis and chills
   b. Fever, headache and constipation
   c. Flatulence, heartburn, abdominal pain and vomiting
   d. Vomiting, dyspepsia and gastrointestinal bleeding

7. The recommended adult starting dose for naloxegol is ____.
   a. 12.5 mg orally once daily
   b. 24 mcg orally twice daily
   c. 25 mg orally once daily
   d. 450 mg orally once daily

8. Naloxegol is contraindicated in patients ____.
   a. taking opioid medications
   b. with diabetes mellitus
   c. with known or suspected GI obstruction
   d. with moderate hepatic impairment

9. A drug-drug interaction between lubiprostone and methadone results in ____.
   a. increased activation of chloride channels in the gut
   b. increased opioid withdrawal
   c. reduced activation of chloride channels in the gut
   d. reduced opioid withdrawal

10. Which of the following is true?
    a. Patients may be reluctant to discuss constipation with their physician.
    b. Pharmacists have no role in helping patients manage OIC.
    c. Pharmacists should not counsel patients about the possibility of OIC if the opioid dose is relatively low.
    d. Pharmacists should not suggest lifestyle modifications to prevent OIC.

Keep the TOP portion for your records. Return the BOTTOM portion to the NPA office. Or, take this quiz online at www.npharm.org

Name ____________________________________________
Mailing Address ____________________________________
City/State/Zip ______________________________________

Circle one (1) Answer:
1. a  b  c  d  
2. a  b  c  d  
3. a  b  c  d  
4. a  b  c  d  
5. a  b  c  d  
6. a  b  c  d  
7. a  b  c  d  
8. a  b  c  d  
9. a  b  c  d  
10. a  b  c  d

CPE Home Study Evaluation
1. Rate this lesson: (Excellent) 5 4 3 2 1 (Poor)
2. Did this lesson meet each of its objectives? ___ Yes ___ No
3. Was the content without commercial bias? ___ Yes ___ No
   If not, please explain_________________________________________________________
4. Did the lesson meet your educational/practice needs? ___ Yes ___ No
5. Comments/future topics are welcome. ________________________________________

The deadline for this quiz is December 12, 2018.
### Legislative Bill Summary

**One Hundred Fifth Legislature, Second Session**

**March 30, 2018**

Not all of the bills introduced to the 2018 Legislative Session are listed below. If you have any questions about a bill not shown, call the Legislative Bill Room at (402) 471-0617 to request a copy of a bill or visit the Nebraska Unicameral web site at [www.nebraskalegislature.gov](http://www.nebraskalegislature.gov).

<table>
<thead>
<tr>
<th>Bill Number</th>
<th>Sponsor</th>
<th>Committee</th>
<th>Hearing Date</th>
<th>Bill Title</th>
<th>Summary</th>
<th>Position</th>
<th>Bill Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>LB 36</td>
<td>Senator Harr</td>
<td>Gov’t-Military &amp; Veterans Affairs Committee</td>
<td>1/20/2017</td>
<td>Administrative Procedure Act/Agency Review of Occupational Credentials</td>
<td>Would require state agencies to review rules and regulations pertaining to the issuance of occupational credentials and to complete and release a critical assessment document (a statement developed by an agency which lacks the force of law but provides a critical analysis of the significance and necessity of the agency’s rules and regulations pertaining to the issuance of all occupational credentials). Would require reviews beginning January 1, 2018 and every year thereafter. Would require a critical assessment document to state and explain a) the health, well-being or consumer protection purpose of the rule or regulation with respect to the issuance of occupational credentials; b) the protection provided by the rule or regulation with respect to the issuance of occupational credentials; c) a review and determination that the rule or regulation has achieved the purpose in a cost-effective manner without unduly inhibiting entrepreneurship and commerce; and d) a description, including an estimated quantification, of the fiscal impact on state agencies, political subdivisions, and regulated persons of the rule or regulation.</td>
<td>Support</td>
<td>In Committee</td>
</tr>
<tr>
<td>LB 44</td>
<td>Senator Watermeier</td>
<td>Revenue Committee</td>
<td>1/27/2017</td>
<td>Remote Seller Sales Tax Collection Act</td>
<td>Would require a Remote Seller (any person who sells tangible personal property, products delivered electronically, or services for delivery into Nebraska and who does not have a physical presence in this state) to remit sales taxes due on sales as if the remote seller had a physical presence in Nebraska, if the remote seller’s gross revenue on sales in Nebraska exceeds $100,000 or involves 200 or more separate sales transactions. Would also require a remote seller refusing to collect Nebraska sales tax to notify Nebraska purchasers that sales or use taxes due on their purchases; send notification to all Nebraska purchasers by January 31 of each year showing the total amount paid by the purchaser for Nebraska purchases from the remote seller; and file an annual statement for each purchaser with the Department of Revenue showing the total amount for Nebraska purchases by such purchasers during the preceding calendar year. [Senator Watermeier Priority Bill]</td>
<td>Support</td>
<td>Final Reading with Amendment</td>
</tr>
<tr>
<td>LB 73</td>
<td>Senator Riepe</td>
<td>General Affairs Committee</td>
<td>2/13/2017</td>
<td>Sale of Tobacco, Vapor Products and Alternative Nicotine Products</td>
<td>Would prohibit the sale to, or use by persons under 21 years of age of tobacco, vapor products, and alternative tobacco products.</td>
<td>Watch</td>
<td>In Committee</td>
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<tr>
<td>LB 117</td>
<td>Senator Hilkemann</td>
<td>Health &amp; Human Services Committee</td>
<td>1/27/2017</td>
<td>Investigational Drug Use Act</td>
<td>Would authorize a manufacturer of an investigational drug, biological product, or device (successfully completed Phase I of a clinical trial, but has not yet been approved for general use by the FDA) to make the treatment available to an eligible patient (person with an advanced illness, attested by the person’s treating physician, who has considered all other treatment options approved by the FDA, has a recommendation from his or her treating physician for use of the investigational drug, biological product, or device, has given written, informed consent for the use of the investigational drug, biological product, or device and has documentation from his or her treating physician that he or she meets the requirements of the Act). Would prohibit revocation, failure to renew, suspension, or any other action against a healthcare provider’s license based solely on the healthcare provider’s recommendation to an eligible patient regarding access to or treatment with an investigational drug, biological product, or device. [Speaker Priority Bill]</td>
<td>Watch</td>
<td>Select File</td>
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<tr>
<td>LB 165</td>
<td>Senator Brewer</td>
<td>Judiciary Committee</td>
<td>2/22/2017</td>
<td>Federal Immigration Verification System</td>
<td>Would require every employer making payment of wages subject to withholding to register with the Tax Commissioner and be assigned a state employer identification number. Would also require such employers to register with and use the federal immigration verification system to determine the work eligibility status of new employees subject to withholding and physically performing services within the state of Nebraska.</td>
<td>Oppose</td>
<td>In Committee</td>
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<td>Bill Number</td>
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<td>LB 324</td>
<td>Senator Kolterman</td>
<td>Banking, Commerce &amp;</td>
<td>2/27/2017</td>
<td>Pharmacy Benefit Fairness and Transparency Act</td>
<td>Support In Committee</td>
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<td></td>
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<td>Insurance Committee</td>
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<td>(1) Would require a pharmacy benefit manager to obtain a certificate of</td>
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<td>authority as a third-party administrator and be subject to the Third-Party</td>
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<td>Administrator Act and Pharmacy Benefit Fairness and Transparency Act;</td>
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<td>(2) Would require a pharmacy benefit manager, within seven days after price</td>
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<td>increase or decrease notification by a manufacturer, supplier, or nationally</td>
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<td>recognized source, to adjust its payment to the contacted pharmacy</td>
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<td>consistent with the price increase or decrease; (3) Would require a</td>
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<td>pharmacy benefit manager to accept into its network any pharmacy or</td>
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<td>pharmacist in good standing and prohibit exclusion of a Nebraska pharmacy</td>
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<td>from participation in its specialty pharmacy network, provided the pharmacy</td>
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<td>is willing to accept the terms of the pharmacy benefit manager’s agreement</td>
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<td>with its specialty pharmacy’s and prohibit requiring a pharmacist or</td>
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<td>pharmacy to participate in one contract with a pharmacy benefit manager</td>
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<td>in order to participate in other contracts with the same pharmacy benefit</td>
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<td>manager; (4) Would prohibit the charging of fees or higher co-pays by</td>
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<td>covered individuals who use a mail-order pharmacy in order to utilize a</td>
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<td>contracted pharmacy or to prohibit a pharmacist or contract pharmacy from</td>
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<td>mailing a prescription drug to a covered individual; (5) Would require a</td>
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<td>pharmacy benefit manager to make readily available to the Director of</td>
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<td>Insurance and to each contracted pharmacy information related to the</td>
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<td>pharmacy benefit manager’s pricing methodology and reimbursement amount</td>
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<td>for single-source and multiple-source prescription drugs and compounds</td>
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<td>and specialty drugs; (6) Would require the reimbursement amount for</td>
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<td>prescription drugs to be updated no less than every seven days by the</td>
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<td>pharmacy benefit manager; (7) Would require all financial benefits (rebates</td>
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<td>, discounts, credits, fees, grants, chargeback’s, or other payments or</td>
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<td>financial benefits of any other kinds) the pharmacy benefit manager</td>
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<td>receives to be disclosed to the covered entity with which the pharmacy</td>
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<td>benefit manager contracts and to disclose to the covered entity and to the</td>
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<td>contracted pharmacy the method used to calculate total dispensing fees,</td>
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<td>the cost of the prescription drug, administrative fees, and any other fee</td>
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<td>payment; (8) Would prohibit a pharmacy benefit manager from charging</td>
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<td>contracted pharmacy’s transaction-based or claims-processing fees; (9)</td>
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<td>Would require benefits payable under a pharmacy benefits management plan</td>
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<td>to be paid within 20 days after receipt of a clean claim, if submitted</td>
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<td>electronically, or 30 days after receipt, if the claim is submitted in</td>
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<td>paper format; (10) Would prohibit adjudication of a clean claim from being</td>
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<td>audited unless fraud is suspected and establishes the manner in which an</td>
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<td>audit of a contracted pharmacies records by a pharmacy benefit manager is</td>
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<td>to be conducted (two-weeks prior notice; conducted by or in consultation</td>
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<td>with a pharmacist employed by a pharmacy benefit manager; cover period not</td>
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<td>to exceed two years from the date on which the claim was submitted to or</td>
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<td>adjudication; not conducted during the first seven calendar days of any</td>
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<td>month and establish an appeals process); and (11) Would authorize sharing</td>
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<td>of information regarding the cost, price, or co-payment of prescription</td>
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<td>drug with a covered individual or covered individual’s caregiver by a</td>
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<td>pharmacist or contracted pharmacy without being subject to penalties or</td>
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<td>removal from a network or plan.</td>
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<tr>
<th>Bill Number</th>
<th>Sponsor</th>
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<th>Hearing Date</th>
<th>Description</th>
<th>Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>LB 402</td>
<td>Senator Hilkemann</td>
<td>Health &amp; Human Services</td>
<td>2/15/2017</td>
<td>Nebraska Regulation of Health Professions Act</td>
<td>Watch In Committee</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Committee</td>
<td></td>
<td>Would change provisions of the Nebraska Regulation of Health Professions Act.</td>
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<tbody>
<tr>
<td>LB 408</td>
<td>Senator Lowe</td>
<td>Business &amp; Labor Committee</td>
<td>3/6/2017</td>
<td>Workers’ Compensation/Evidenced-Based Drug Formulary</td>
<td>Support In Committee</td>
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<td>Would establish an evidence-based drug formulary consisting of Schedule II,</td>
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<td>III, IV and V prescription drugs in connection with workers compensation</td>
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<td>claims with a date of injury on or after January 1, 2018.</td>
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<tr>
<td>LB 420</td>
<td>Senator McCollister</td>
<td>Business &amp; Labor Committee</td>
<td>3/13/2017</td>
<td>Fair Chance Hiring Act</td>
<td>Oppose General File with Amendment</td>
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<td>Would prohibit public and private employers and employment agencies from</td>
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<td>asking an applicant to disclose, orally or in writing, information</td>
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<td>concerning the applicant’s criminal record or history, including any inquiries</td>
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<td>on any employment application, until the employer or employment agency</td>
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<td>has determined the applicant meets the minimum employment qualifications.</td>
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<td>Would apply to employers with 15 or more employees.</td>
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<tr>
<th>Bill Number</th>
<th>Sponsor</th>
<th>Committee</th>
<th>Hearing Date</th>
<th>Description</th>
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<tr>
<td>LB 438</td>
<td>Senator Howard</td>
<td>Revenue Committee</td>
<td>3/17/2017</td>
<td>Cigarette Tax</td>
<td>Watch In Committee</td>
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<td>Would increase cigarette and tobacco taxes as prescribed and provide for the</td>
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<td>distribution of funds.</td>
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<tr>
<td>Bill Number</td>
<td>Sponsor</td>
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<td>LB 441</td>
<td>Senator Morfeld</td>
<td>3/8/2017</td>
<td>Medicaid Expansion</td>
<td>Would change eligibility provisions under the Medical Assistance Act.</td>
<td>Support</td>
</tr>
<tr>
<td>LB 473</td>
<td>Senator Walz</td>
<td>3/13/2017</td>
<td>Mandated Employee Rest Periods</td>
<td>Would require employers employing six or more individuals to allow employees a rest period of at least 15 minutes during each four hours worked, in addition to the regular scheduled lunch period for the employees.</td>
<td>Watch</td>
</tr>
<tr>
<td>LB 474</td>
<td>Senator Baker</td>
<td>2/13/2017</td>
<td>Synchronized Medications</td>
<td>Would require insurance coverage for filling prescriptions to synchronize the patients' medications. Would require any insurance policy providing coverage for prescription medications to apply a prorated daily cost-sharing rate to prescriptions that are dispensed by a network pharmacy for a partial supply if the prescribing practitioner or pharmacist determines the fill or refill to be in the best interest of the patient and the patient requests or agrees to a partial supply for the purpose of synchronizing the patient's medications. Would authorize a pharmacy to override any denial codes indicating that a prescription is being refilled too soon for purposes of medication synchronization and would require dispensing fees for partially filled or refilled prescriptions to be paid in full for each prescription dispensed, regardless of any prorated daily cost-sharing for the beneficiary for fees paid for alignment services.</td>
<td>Support</td>
</tr>
<tr>
<td>LB 586</td>
<td>Senator Linehan</td>
<td>3/23/2017</td>
<td>Prescription Drug Monitoring Program</td>
<td>Would authorize a dispenser or any licensed or registered health care profession designated by a dispenser to act as an agent for the dispenser for purposes of submitting or accessing data in the prescription drug monitoring system provided the designee is directly supervised by the dispenser.</td>
<td>Oppose</td>
</tr>
<tr>
<td>LB 622</td>
<td>Senator Wishart</td>
<td>3/15/2017</td>
<td>Medical Cannabis Act</td>
<td>Would authorize the use of marijuana for medicinal purposes.</td>
<td>Watch</td>
</tr>
<tr>
<td>LB 661</td>
<td>Senator Kuehn</td>
<td>2/9/2017</td>
<td>Confidentiality of Information Relating to Lethal Injection</td>
<td>Would make records containing any information that would lead to the identity of any person or entity that manufactures, supplies, compounds, or prescribes the substance or substances, medical supplies, or medical equipment utilized to perform a lethal injection confidential and exempt from disclosure.</td>
<td>Watch</td>
</tr>
<tr>
<td>LB 701</td>
<td>Senator Koltermann</td>
<td>1/26/2018</td>
<td>Uniform Credentialing Act - Telehealth Practice</td>
<td>Would authorize a physician or a physicians assistant to establish a provider-patient relationship through telehealth (use of medical information electronically exchanged from one site to another, whether synchronously or asynchronously, to aid a credential holder in the diagnosis or treatment of a patient).</td>
<td>Watch</td>
</tr>
<tr>
<td>LB 731</td>
<td>Senator Williams</td>
<td>1/18/2018</td>
<td>Remote Dispensing Pharmacies</td>
<td>Would authorize remote dispensing by pharmacies in Nebraska to enhance access to pharmacies/pharmacist in rural and under-served areas of Nebraska. Would require the remote dispensing pharmacy to be staffed by a certified pharmacy technician, owned by a supervising pharmacy (licensed and located in Nebraska) and located no less than 10 driving miles from another pharmacy. Would require a pharmacist in charge (PIC) of the supervising pharmacy to also serve as the PIC for the remote dispensing pharmacy and require a real-time audio/visual connection to be operational in order for dispensing to occur. Would allow the PIC to delegate tasks to a &quot;virtual pharmacist,&quot; such as supervision, verification, DUR, patient counseling, etc., but would require the &quot;virtual pharmacist&quot; to be employed by the supervising pharmacist. Would require the pharmacist to attempt to counsel or provide a new prescriptions dispensed from a remote dispensing pharmacy to a patient. [HHS Committee Priority Bill]</td>
<td>Support</td>
</tr>
<tr>
<td>LB 788</td>
<td>Senator Riepe</td>
<td>1/18/2018</td>
<td>Uniform Credentialing Act</td>
<td>Would require, with the first license renewal period beginning on or after October 1, 2018, the continuing competency requirements for a nurse, midwife, nurse anesthetist, dentist, physician, physician assistant, nurse practitioner, podiatrist, and veterinarian to include at least five hours of continuing education biennially regarding prescribing opiates, with at least two of the five hours of continuing education to cover the Prescription Drug Monitoring Program.</td>
<td>Watch</td>
</tr>
<tr>
<td>LB 789</td>
<td>Senator Ebke</td>
<td>1/24/2018</td>
<td>Marijuana and Controlled Substances Tax</td>
<td>Would repeal the marijuana and controlled substances tax presently imposed on dealers.</td>
<td>Watch</td>
</tr>
<tr>
<td>Bill Number</td>
<td>Committee</td>
<td>Hearing Date</td>
<td>Title</td>
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<tr>
<td>LB 798</td>
<td>Revenue Committee</td>
<td>Hearing 2/14/2018</td>
<td>Sales Taxation</td>
<td>Watch In Committee</td>
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<tr>
<td>LB 832</td>
<td>Judiciary Committee</td>
<td>Hearing 1/26/2018</td>
<td>Uniform Controlled Substances Act</td>
<td>Watch General File with Amendment</td>
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<tr>
<td>LB 834</td>
<td>Health &amp; Human Services Committee</td>
<td>Hearing 1/24/2018</td>
<td>Uniform Credentialing Act</td>
<td>Watch In Committee</td>
<td></td>
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<tr>
<td>LB 837</td>
<td>Executive Board</td>
<td>Hearing 1/25/2018</td>
<td>Medical Assistance Act</td>
<td>Support In Committee</td>
<td></td>
</tr>
<tr>
<td>LB 843</td>
<td>Business &amp; Labor Committee</td>
<td>Hearing 2/12/2018</td>
<td>Nebraska Wage Payment and Collection Act</td>
<td>Watch In Committee</td>
<td></td>
</tr>
<tr>
<td>LB 844</td>
<td>Business &amp; Labor Committee</td>
<td>Hearing 2/12/2018</td>
<td>Healthy and Safe Families and Workplace Act</td>
<td>Watch In Committee</td>
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<tr>
<td>LB 862</td>
<td>Health &amp; Human Services Committee</td>
<td>Hearing 2/22/2018</td>
<td>Prescription Drug Cost Transparency Act</td>
<td>Watch In Committee</td>
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<tr>
<td>LB 866</td>
<td>Health &amp; Human Services Committee</td>
<td>Hearing 2/14/2018</td>
<td>Medical Assistance Act</td>
<td>Support In Committee</td>
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**Sales Taxation**
Would provide a sales and use tax exemption for feminine hygiene products.

**Uniform Controlled Substances Act**
Would change the definition of marijuana to exclude any material, preparation, mixture, compound, or other substance which contains 10 percent or less cannabidiol by weight and three-tenths of one percent or less tetrahydrocannabinols by weight.

**Uniform Credentialing Act**
Would authorize the waiver of all initial occupational fees and fees from licensing requirements for low-income individuals, military families, and young workers.

**Medical Assistance Act**
Would require submission of waiver applications to the Health and Human Services Committee of the Legislature prior to submitting the application to the Federal Centers for Medicare and Medicaid Services. Would require the Health and Human Services Committee to hold a public hearing within 90 days after submission of the application to the Committee and either approve or disapprove submission of the application to the Federal Centers for Medicare and Medicaid Services.

**Nebraska Wage Payment and Collection Act**
Would prohibit an employer from requiring non-disclosure of wages as a condition of employment and prevent an employer from requiring an employee to sign a waiver or other document purporting to deny an employee the right to disclose the employees wages. Would prohibit an employer from taking any adverse employment action against an employee for disclosing an employee’s own wages or discussing another employee’s wages that have been disclosed voluntarily. Would establish a cause of action under the Nebraska Wage and Payment and Collection Act for violations by an employer with the employee entitled to receive reinstatement, back pay, restoration of loss service credit, money damages and costs and reasonable attorney’s fees.

**Healthy and Safe Families and Workplace Act**
Would allow employees to accrue a minimum of one hour of paid sick time for every 30 hours worked, with a maximum of 40 hours of paid sick time accrued in a calendar year. Under the measure, employees would be entitled to use accrued paid sick time beginning on the 60th calendar day following commencement of employment. Paid sick leave would be authorized for a) an employee’s mental or physical illness, injury, or health condition; b) an employee’s need for medical diagnosis, care, or treatment of a mental or physical illness, injury, or health condition; c) an employee’s need for preventative medical care; d) care of a family member with a mental or physical illness, injury, or health condition; e) care of a family member who needs medical diagnosis, care, or treatment of a mental or physical illness, injury, or health condition; f) care of a family member who needs preventative medical care; or g) absence necessary due to domestic assault, sexual assault, or stalking.

**Prescription Drug Cost Transparency Act**
Would a) require notice and disclosure of information relating to the cost and pricing of prescription drugs in order to provide accountability to the State for prescription drug pricing; b) permit a manufacturer of a prescription drug to voluntarily make pricing decisions regarding the prescription drug, including any price increases; and c) permit both private and public purchasers of prescription drugs to negotiate discounts and rebates for prescription drugs consistent with state and federal law. Would require a manufacturer of a prescription drug with a wholesale acquisition cost of more than $40 for a course of therapy to provide notice to specified individuals if the increase in the wholesale acquisition cost of a prescription drug is more than 16 percent, including the proposed increase and any cumulative increase within the previous two calendar years prior to the year in which the sale is made. Would require entities to register with the Department of Administrative Services in order to receive notifications (notice required to be provided within writing at least 60 days prior to planned effective date of the increase). Would require pharmacy benefit managers receiving notice to notify contracting public and private purchasers which provide coverage for more than 500 lives of the increase.

**Medical Assistance Act**
Would require the Health and Human Services Committee to hold a hearing within 90 days of receiving reports pertaining to the Medicaid State Plan amendments or waivers to conduct a public hearing (DHHS to be represented by the Director of Medicaid and Long-Term Care or the Chief Executive Officer of the Department). Would require the Department to provide a public notice and comment period prior to submitting an application for or extension or elimination of Medicaid waiver.
<table>
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<th>Bill Number</th>
<th>Sponsor</th>
<th>Committee</th>
<th>Hearing Date</th>
<th>Description</th>
<th>Status</th>
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<tr>
<td>LB 867</td>
<td>Senator Crawford</td>
<td>Health &amp; Human Services Committee</td>
<td>2/14/2018</td>
<td>Managed Care</td>
<td>Support In Committee</td>
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<tr>
<td>LB 906</td>
<td>Senator Williams</td>
<td>Judiciary Committee</td>
<td>1/26/2018</td>
<td>Uniform Controlled Substance Act</td>
<td>Support Final Reading</td>
</tr>
<tr>
<td>LB 913</td>
<td>Senator McDonnell</td>
<td>Judiciary Committee</td>
<td>1/31/2018</td>
<td>Assault of Healthcare Practitioners</td>
<td>Support Signed by Speaker</td>
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<tr>
<td>LB 923</td>
<td>Senator Morfeld</td>
<td>Judiciary Committee</td>
<td>1/31/2018</td>
<td>Administration of Naloxone</td>
<td>Watch Final Reading</td>
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<tr>
<td>LB 924</td>
<td>Senator Riepe</td>
<td>Health &amp; Human Services Committee</td>
<td>1/24/2018</td>
<td>Uniform Credentialing Act</td>
<td>Watch General File with Amendment</td>
</tr>
<tr>
<td>LB 931</td>
<td>Senator Howard</td>
<td>Judiciary Committee</td>
<td>1/26/2018</td>
<td>Opioid Prescriptions for Minors</td>
<td>Watch Signed by Speaker</td>
</tr>
<tr>
<td>LB 932</td>
<td>Senator Howard</td>
<td>Judiciary Committee</td>
<td>2/1/2018</td>
<td>Opioid Treatment</td>
<td>Watch In Committee</td>
</tr>
<tr>
<td>LB 933</td>
<td>Senator Lindstrom</td>
<td>Judiciary Committee</td>
<td>1/26/2018</td>
<td>Opioid Prescriptions</td>
<td>Watch General File Amended into LB 931</td>
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**Opioid Prescriptions**

Would require a practitioner prescribing a controlled substance listed in Schedule II of section 28-405 or any other opiate not listed in Schedule II, prior to issuing the initial prescription for a course of treatment for acute or chronic pain and again prior to the third prescription for such course of treatment, to discuss with the patient, or the patient’s parent or guardian if the patient is younger than 18 years of age and is not emancipated, (a) The risks of addiction and overdose associated with the controlled substance or opiate being prescribed, including, but not limited to: (i) Controlled substances and opiates are highly addictive even when taken as prescribed; (ii) There is a risk of developing a physical or psychological dependence on the controlled substance or opiate; and (iii) Taking more controlled substances or opiates than prescribed, or mixing sedatives, benzodiazepines, or alcohol with controlled substances or opiates, can result in fatal respiratory depression; (b) The reasons why the prescription is necessary; and (c) Alternative treatments that may be available.
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<tr>
<td>LB 934</td>
<td>Senator Kuehn</td>
<td>Judiciary Committee</td>
<td>1/26/2018</td>
<td><strong>Opioid Prescriptions</strong> Would require a customer, in order to take receipt of dispensed opiates listed in Schedule II, III or IV of section 28-405 to display a valid driver’s or operator’s license, a Nebraska state identification card, a military identification card, an alien registration card, or a passport as proof of identification.</td>
<td>Oppose</td>
<td>General File Amended into LB 931</td>
</tr>
<tr>
<td>LB 970</td>
<td>Senator Wayne</td>
<td>Judiciary Committee</td>
<td>1/26/2018</td>
<td><strong>Uniform Controlled Substances Act-Marijuana Penalties</strong> Would establish a Class IV felony for persons manufacturing or distributing marijuana in a quantity of one ounce or less and a Class IIA felony for cases involving more than one ounce of marijuana.</td>
<td>Watch</td>
<td>In Committee</td>
</tr>
<tr>
<td>LB 971</td>
<td>Senator Wayne</td>
<td>Judiciary Committee</td>
<td>1/26/2018</td>
<td><strong>Uniform Controlled Substances Act-Penalties for Possession of Controlled Substances</strong> Would establish a Class I misdemeanor penalty for the possession of marijuana weighing up to and including one gram, or if the controlled substances is in the amount of fewer than 10 pills or tablets weighing no more than 80 milligrams each and a Class IV felony in cases involving controlled substances in an amount weighing more than one gram but less than 10 grams, or if the controlled substances in the amount of 10 pills or tablets or more, but weighing less than 10 grams.</td>
<td>Watch</td>
<td>General File with Amendment</td>
</tr>
<tr>
<td>LB 1057</td>
<td>Senator Kuehn</td>
<td>Health &amp; Human Services Committee</td>
<td>2/23/2018</td>
<td><strong>Prescription Drug Monitoring Program</strong> Would, for purposes of the Prescription Drug Monitoring Program define “dispensed prescription” to mean a prescription drug delivered to the ultimate user by or pursuant to the lawful order of the prescriber, not including a) delivery of such prescription drug for immediate use for purposes of inpatient hospital care or emergency department care; b) the administration of a prescription drug by an authorized person upon the lawful order of a prescriber; c) a wholesale distributor of a prescription drug monitored by the prescription drug monitoring system; or d) the dispensing to a nonhuman patient of a prescription drug which is not a controlled substance listed in Schedule II, Schedule III, Schedule IV, or Schedule V of Section 28-405.</td>
<td>Watch</td>
<td>General File Amended into LB 1034</td>
</tr>
<tr>
<td>LB 1062</td>
<td>Senator McDonnell</td>
<td>Appropriations Committee</td>
<td>2/15/2018</td>
<td><strong>Tobacco Prevention and Control Program</strong> Would express the intent of the Legislature to include an additional $2,400,000 for the Tobacco Prevention and Control Program from the Nebraska Health Care Cash Fund for Fiscal year 2018-19.</td>
<td>Watch</td>
<td>In Committee</td>
</tr>
<tr>
<td>LB 1063</td>
<td>Senator McDonnell</td>
<td>Transportation Committee</td>
<td>2/13/2018</td>
<td><strong>Brain Injuries</strong> Would create the Brain Injury Cash Fund for use to pay for contracts for assistance for victims of traumatic brain injury with outside sources that specialize in the area of traumatic brain injury. Would increase certain operators license fees to provide revenue for the Brain Injury Cash Fund.</td>
<td>Watch</td>
<td>In Committee</td>
</tr>
<tr>
<td>LB 1093</td>
<td>Senator Walz</td>
<td>Health &amp; Human Services Committee</td>
<td>2/13/2018</td>
<td><strong>Inspector General of Nebraska Public Health</strong> Would create the Office of Inspector General of Nebraska Public Health within the office of public counsel for the purpose of conducting investigations, audits, inspections, and other reviews of state shown facilities providing health care and state-licensed health care facilities.</td>
<td>Watch</td>
<td>In Committee</td>
</tr>
<tr>
<td>LB 1117</td>
<td>Senator Crawford</td>
<td>Revenue Committee</td>
<td>2/21/18</td>
<td><strong>Cigarette Tax</strong> Would increase the tax on a pack of cigarettes from 64 cents to 2.14 cents.</td>
<td>Watch</td>
<td>In Committee</td>
</tr>
<tr>
<td>LB 1119</td>
<td>Senator Riepe</td>
<td>Gov’t-Military &amp; Veterans Affairs Committee</td>
<td>2/7/2018</td>
<td><strong>Direct Primary Care Pilot Program Act</strong> Would authorize the establishment of a Direct Primary Care Pilot Program (involves health plans which include primary care services provided by a participating provider and health care coverage for medical specialist, hospitals, pharmacy, and other medical coverage. Would provide for the pilot program to run from fiscal year 2019-20 through fiscal year 2021-22 and establish the program within the Nebraska State Insurance Program. [Senator Hilgers Priority Bill]</td>
<td>Support</td>
<td>Final Reading</td>
</tr>
<tr>
<td>LB 1127</td>
<td>Senator Kolterman</td>
<td>Health &amp; Human Services Committee</td>
<td>2/21/18</td>
<td><strong>Uniform Credentialing Act</strong> Would authorize additional fees for each applicant for the initial issuance and renewal a credential to practice (including pharmacists) of $10 annually for a patient safety fee. Would transfer fees to the patient safety cash fund to support the activities of a patient safety organization.</td>
<td>Watch</td>
<td>General File</td>
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The Opioid Crisis
Focusing on Drug Interactions

Objectives
At the conclusion of this lesson, pharmacists and pharmacy technicians should be able to:
1. Identify opioid adverse events and contraindications.
2. Describe the effect of CYP450 enzymes' polymorphism on opioid metabolism.
3. List drug classes that inhibit CYP450 enzymes and their effects on opioid metabolism.

Introduction
Opioid agonists are a class of drugs that occur naturally and can be produced synthetically. Morphine and codeine are naturally occurring opioids which come from the opium poppy plant. There are many semi-synthetic and synthetic opioids that are used as pain-relieving drugs such as hydrocodone, oxycodone, and fentanyl. Morphine is the benchmark of opioid analgesia and the agent to which all other analgesics are compared. Opioids can also be classified according to their effect on opioid receptors (mu, delta, kappa, zeta and nociception opioid peptide receptor). Opioid agonists interact with the receptors to produce a response, while opioid antagonists interact with the receptors without producing any response but prevent an agonist from binding to the receptor. All opioids bind to opioid receptors in the human body and brain to cause their pharmacological effect. Analgesia is the primary medical use for opioids, however, opioids also have secondary uses such as suppression of diarrhea or cough.¹

Over the course of a given year, approximately 100 million people in the United States who suffer from pain could benefit from appropriate pain management by using opioids in conjunction with other methods of treatment.² Prescribing of opioids has increased and been associated with misuse and overdose. Opioid adverse drug reactions are most often caused by the opioid itself but can also be a result of the interaction of the opioid and another drug. The National Center for Diseases Control and Prevention (CDC) analysis of 2014 reported the rate of drug overdose deaths increased significantly for both sexes, in persons aged 24 to 44 years and over 55 years in the northeastern, midwestern, and southern regions of the United States. The rate of opioid overdose deaths also increased by 14% from 7.9 per 100,000 in 2013 to 9 per 100,000 in 2014.³⁴

In April 2017, the Food and Drug Administration (FDA) updated a new warning against the use of codeine and tramadol in children younger than 12 years. For children aged 12 to 18 years, the FDA warns against the use of codeine and tramadol if there is a history of obesity, obstructive sleep...
apnea, or severe lung disease. Neither codeine nor tramadol should be given to children or adolescents as a pain medication after surgery to remove tonsils or adenoids. The FDA also warns against the use of such drugs in breastfeeding women because of the possibility of the drug being excreted in breastmilk and causing harm to infants. In January of 2018, the FDA updated these recommendations to limit the use of codeine and hydrocodone in patients under 18 years of age.

**Warnings and Contraindications of Opioids**

Recent literature suggests that the combined use of opioid medicines with benzodiazepines, acetaminophen, or other drugs that depress the central nervous system (CNS) is rapidly growing resulting in serious side effects including liver toxicity, respiratory depression, and death. The FDA has added boxed warnings to the drug labeling of prescription opioid pain medicines and benzodiazepines about use of these drug classes together. Based on a Veterans Health Administration (VHA) study, the combination of opioids and benzodiazepines is associated with an increased risk of death from drug overdose. During a VHA study period, 27% (n=420,386) of veterans who received opioid analgesics also received a benzodiazepine. In the study, about half of the deaths (n=1185) from drug overdose occurred when veterans were concurrently using benzodiazepines and opioids (with adjusted hazard ratio 2.33; 95% CI 2.05 to 2.64). The VHA study also showed that the risk of death from drug overdose increased as daily benzodiazepine dose increased. The combination of acetaminophen and opioid drugs such as oxycodone, hydrocodone, codeine, and tramadol have always included a boxed warning about the risks of hepatotoxicity, serious skin reaction or hypersensitivity to acetaminophen. In addition, there are warnings about the misuse, abuse, and diversion of opioids. Opioids are contraindicated for patients with significant respiratory depression, acute or severe bronchial asthma, head injury, and increased intracranial pressure.

**Adverse Effects of Opioids**

All opioid agonists have the potential for misuse, abuse, and overdose. Their use should be monitored closely, particularly for the long acting agents such as extended-release morphine, fentanyl patches, extended-release oxycodone, and methadone due to their long duration of action. As opioids work on opioid receptors in the brain (mu, delta, and kappa), they can affect the CNS and cause side effects such as drowsiness, somnolence, confusion, and dizziness. Other common side effects include constipation, nausea, vomiting, pruritis and headache. Acute overdose with morphine and other opioids is manifested by respiratory depression, somnolence progressing to stupor or coma, shivering, constricted pupils, pulmonary edema, bradycardia, hypotension, and death. Respiratory depression experienced during opioid overdose occurs due to decreasing sensitivity to carbon dioxide in the brainstem.

Studies have also found that naturally occurring opioids diminish testosterone levels by inhibiting both hypothalamic gonadotropin releasing hormone (GnRH) production and testicular testosterone synthesis. To assess this effect, a study was conducted on 54 men consuming oral sustained-action dosage forms of opioids several times daily for control of nonmalignant pain. During the study period, in the patients who took opioids, the hormone levels were measured and compared with 27 similar men consuming no opioids. It was found that the average hormone level was much lower in opioid users than in control subjects in dose-related patterns (p-value < 0.001) for all comparisons.

Narcotic bowel syndrome (NBS) and opioid induced-constipation (OIC) are other examples of opioid adverse reactions. OIC may occur within a few days after initiating opioids and can exacerbate existing constipation. Activation of mu receptors in the gastrointestinal tract (GI) after opioid administration decreases the motility of the GI tract by slowing gastric emptying and reduces the propulsive contractions of the small intestine and colon. The combination of these effects leads to symptoms of constipation. NBS is characterized by the development of worsening abdominal pain linked to chronic use or escalating doses of opioids. Studies have found that with chronic use of opioids, tolerance can develop for the analgesic effect with sensitization of excitatory response that is generated by glial cells at the levels of both spinal cord and opioid transmembrane receptors leading to paradoxical hyperalgesia. Treatment of NBS may involve inpatient medical hospitalization with careful opioid tapering using intravenous morphine, reducing the dose each day by 15 to 33%. During the NBS treatment which lasts 4 to 10 days, patients receive an antidepressant for non-opioid pain control, medium to long-acting benzodiazepines for anxiety and clonidine for withdrawal symptoms. In case of OIC, the treatment is typically approached in a stepwise fashion starting with lifestyle modifications such as increased physical activity and increased fluid intake. Fiber supplementation and polyethylene glycol (PEG) are the most effective nonprescription therapies for OIC. The favorable side effect profile and low
cost of PEG makes it a good choice for first line treatment with or without a stimulant laxative. Recent drug developments for treatment of OIC have been focused on the peripheral acting mu-opioid receptor antagonists which include methylaltrexone, alvimopan and naloxegol. Mu-opioid receptor antagonists bind to the mu receptors on the gastrointestinal tract without activating them, thereby, preventing opioid binding.11,12,14

Effect of CYP Genetic Polymorphism on Opioid Metabolism

The rate of opioid metabolism is governed by many factors such as genetic makeup, gender, age, diet, patient's disease state, and concurrent use of medications. Opioid metabolism is mostly dependent on the cytochrome P (CYP) 450 enzyme system. These enzymes promote two forms of metabolism: Phase 1 metabolism (oxidation and reduction reactions) and Phase 2 metabolism (conjugation reactions). One important Phase 2 reaction is glucuronidation which metabolizes morphine and its derivatives (oxymorphone and hydromorphone). Genetic factors sometimes play an important role in patients with genetic polymorphism in one or more of their CYP isozymes.15

For example, the polymorphism in CYP2D6 enzyme can be classified according to one of four levels of activity: poor metabolizers (PM), intermediate metabolizers (IM), extensive metabolizers (EM), and ultra-rapid metabolizers (UM). Regarding polymorphism in CYP2D6, the EM is expressed by most of the population to a level that is considered normal, while PM phenotype is expressed by two deficient, inherited alleles (CYP2D6*9, and CYP2D6*10). As a result, patients with PM phenotype metabolize drugs at a notably slower rate which leads to the accumulation of the drugs and toxicity. Patients with UM phenotype carry a CYP2D6 enzyme that expresses multiple copies of the gene which increases the enzyme activity and leads to rapid metabolism of substances. Thus, patients with UM phenotype eliminate drugs at a greater rate which leads to potentially lower drug efficacy at standard dose.16,17

The prevalence of CYP2D6 with PM phenotype varies among ethnic populations. Prevalence of the CYP2D6 enzyme with the PM phenotype in the United States is found to be high in Caucasians (10% of the population), while it is relatively low among Asian (Chinese and Japanese), and slightly higher among the Asian-Indian populations.18 Globally, approximately 5-14% of Caucasians, 0-5% of Africans, and 0-1% of Asians lack CYP2D6 activity. These individuals are known as PMs. The UM phenotype of CYP2D6 is found to be at a low frequency among the European population and a much higher prevalence in populations from countries surrounding the Mediterranean Sea. The highest frequency of UM phenotype is reported in Ethiopians (29%) and Saudi Arabians (21%), while in Caucasians and African Americans it appears in a similar frequency.19

CYP3A4 is responsible for the metabolism of approximately 50% of all currently available prescription medications. Examples of opioids that are metabolized by the CYP3A4 enzyme include methadone and fentanyl.20 There are many forms of CYP enzymes involved in methadone metabolism, but they primarily include: CYP3A4, CYP2B6 and CYP2C9. These multiple interactions between methadone and CYP enzyme contribute to many methadone-drug interactions. Studies have shown that there are no known clinically relevant polymorphisms in CYP3A4, but CYP2D6 and CYP2C9 have genetic mutations with significant effects on drugs efficacy and adverse events. Patients carrying mutations on such CYP enzymes are at risk for exhibiting high methadone concentrations.21,22 Studies have shown that there is a significant relationship between high plasma methadone concentration and QT interval prolongation above the 450 ms threshold. The probability of the QT interval value being above 450 ms was assessed in a study that included 104 patients who were receiving oral methadone maintenance for chronic pain management. The average methadone dose was 110 mg/day (20 – 1200 mg/day). The study resulted in 32% patients with QT prolongation ranging between 394 to 494 ms. The data further suggested that the relationship between methadone dose and cardiac effects may be complex and related to gender and duration of treatment. Furthermore, the risk for QT prolongation could also increase for patients taking methadone at doses exceeding 240 mg/day with a genetic status associated with a decreased methadone elimination or also taking drugs that increase QT interval such as amiodarone and chlorpromazine.23,24

Interactions Between CYP450 Inhibitors/Inducers and Opioids

Drug-drug interactions are a more common issue in clinical practice, especially the interactions that are mediated through CYP450 inhibition or induction. Alteration of CYP450 enzymes can cause unanticipated adverse reactions or therapeutic failures. There are many drug classes that are known to either inhibit or induce CYP450 enzymes. Examples of such classes include: statins, SSRIs,
Table 1 | Selected CYP3A4 Inhibitors and Inducers that Interact with Opioids\textsuperscript{20,30,31}

<table>
<thead>
<tr>
<th>Opioids/CYP Isozymes</th>
<th>CYP3A4 Inhibitors</th>
<th>Type of Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Codeine (CYP3A4 and CYP2D6)</td>
<td>Antibiotics</td>
<td>Decreased rate of opioid metabolism, increased opioid effects, and increased risk of opioid toxicity</td>
</tr>
<tr>
<td>• Norco, Lortab, Vicodin (hydrocodone) (CYP3A4 and CYP2D6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• OxyContin (oxycodone), (CYP3A4 and CYP2D6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Dolophine (methadone), (CYP3A4, CYP2B6, CYP2D6, CYP2C8, CYP2C9 and CYP2C19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Ultram (tramadol) (CYP3A4, CYP2D6 and CYP2B6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Fentanyl (CYP3A4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Food</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Grapefruit juice</td>
<td></td>
</tr>
</tbody>
</table>

Antibiotics
- Biaxin (clarithromycin)
- Cipro (ciprofloxacin)
- Erythromycin
- Rifadin (rifampin)

Antiretrovirals
- Prezista (darunavir/ritonavir)
- Rescriptor (delavirdine)
- Reyataz (atazanavir)

Antifungals
- Diflucan (fluconazole)
- Sporanox (itraconazole)
- Vfend (voriconazole)

Antidepressants
- Serzone (nefazodone)

Chemotherapeutic Agents
- Tamoxifen
- Tykerb (lapatinib)

Other Drugs
- Disulfiram
- Emend (aprepitant)
- Gengraf (cyclosporine)
- Rapamune (sirolimus)
- Tagamet (cimetidine)

Food
- Grapefruit juice

CYP3A4 Inducers

Anticonvulsants
- Dilantin (phenytoin)
- Luminal (phenobarbital)
- Teqetrol (carbamazepine)

Other
- Caffeine
- Decadron (dexamethasone)
- St John’s Wort

Strong induction, increased opioid metabolism and clearance which leads to decreased therapeutic effects

macrolide antibiotics, azole antifungals, anti-HIV agents, antiplatelets, calcium channel blockers (verapamil and diltiazem), steroids, benzodiazepines, beta blockers, and warfarin (Tables 1 and 2). Most opioids are metabolized via CYP450 enzyme system, and they are more prone to drug-drug interactions with commonly prescribed drugs which are also metabolized through such enzymes. For example, codeine is metabolized in the liver by CYP2D6 to morphine. If codeine is co-administered with a drug that inhibits CYP2D6, codeine would not be active to exert its therapeutic action, instead it would accumulate in the body and cause serious adverse events. Some opioids such as oxycodone can be metabolized through two enzymatic pathways (CYP2D6 and CYP3A4). If one pathway is altered, the other would metabolize the drug. If both pathways of oxycodone metabolism are inhibited, the drug will accumulate and serious adverse events would occur. For instance, in studies that assessed the effects of inhibition of both CYP3A4 and CYP2D6 on oxycodone metabolism, it was found that the mean area under the curve (AUC) of oxycodone increased by 2.9-fold when CYP3A4 is inhibited by either ketoconazole or itraconazole (strong CYP450 inhibitors). Available data also indicate that impaired activity of CYP2D6 by its inhibitors or polymorphism is associated with only a small change in oxycodone pharmacokinetics. In another study, the plasma concentration of oxycodone increased by 2.7 to 5.6-fold when co-administered with voriconazole (strong CYP3A4 inhibitors). Fentanyl, buprenorphine, and methadone are other opioids metabolized via CYP3A4. Studies have shown that the risk for side effects due to administration of methadone or buprenorphine with weak to moderate
CYP3A4 inhibitors is limited, but some patients may be more vulnerable if other metabolic pathways are also reduced. When methadone is combined with strong CYP3A4 inhibitors such as clarithromycin, ciprofloxacin, atazanavir, and ritonavir, its plasma concentration may increase more than 5-fold. In the case of buprenorphine, there is no potential for toxicity due to its ceiling effect for opioids receptors.28,29

Common Drugs That Interact with Opioids

Drug-drug interactions (DDIs) are an important and potentially preventable cause of adverse drug reactions. DDIs may alter the pharmacokinetics (absorption, distribution, metabolism, and excretion) of drugs when they are combined. Consequently, loss of efficacy or toxicity of the drug may occur. As a class of drugs, opioids are associated with a narrow therapeutic index, wide interpatient variability in response, and potential for life-threatening toxicity.30

Opioid adverse drug reactions are most often caused by the opioid itself, but can also be a result of the combination of the opioid and another drug. Often, DDIs involving opioids cause various CNS symptoms as well as other systemic complications. Examples of complications include: delirium, serotonin syndrome, hyperalgesia, extrapyramidal symptoms, hypotension, hypertension, vomiting, sweating, ventricular tachycardia/torsade de points, QT interval prolongation, and respiratory depression. Studies have reported many mechanisms of action behind opioid DDIs including inhibition or induction of opioid metabolism through CYP450 enzymes or other
metabolizing enzymes, decreased renal elimination of an opioid, potentiation of analgesic efficacy through opioid and nonopioid mechanisms, inhibition or reversal of the effect of an opioid by antagonism at opioid receptors or modification of cholinergic, adrenergic, dopaminergic, and serotoninergic activity in the CNS (Table 3). Opioids can cause drug interactions in patients who are receiving or who have received monoamine oxidase inhibitors (MAOIs), antimigraine agents, antiemetics, SSRIs and St John's wort within the previous 14 days. The use of opioids with other drugs that have serotoninergic effects could lead to serious, adverse events such as serotonin syndrome, seizures, and respiratory depression.31

### Conclusion

Over the past decade, opioid misuse, abuse, and overdose has increased drastically in the United States.2 Opioid drug-drug interactions occur when opioids are co-administered with drugs that inhibit or induce CYP450 enzymes, as most opioids are prodrugs and depend on enzymatic reaction to be active.31 Notably, the genetic polymorphism on CYP450 enzymes also play a big role in opioid overdose and toxicity.19 The combination of opioids with other drugs that also have CNS effects could lead to serious adverse events such as respiratory depression, hypotension, and death. Therefore, when prescribing opioids, drug-drug interactions should be considered and drugs that have significant DDIs with opioids should be titrated carefully or avoided.

| **Table 3 | Selected Prescription Drugs and Drug Classes that Interact with Opioids**20,30,31,32,33,34 |
|---|---|---|
| **Opioids** | **Drugs/Drug classes** | **Result of the interactions** |
| • Codeine | Axert (almotriptan) | Severe serotonin syndrome, CNS depression, respiratory depression and death |
| • Demerol (meperidine) | Hiprex (methenamine) | |
| • Dolophine (methadone) | Strattera (atomoxetine) | |
| • Duragesic (fentanyl) | SSRIs, SNRIs, St John's Worts and MAOIs | |
| • Lortab (hydrocodone) | MS Contin (morphine) | |
| • OxyContin, Percocet, Percodan, (oxycodone) | Ultram (tramadol) | |
| **Muscle Relaxants** | **Axert (almotriptan)** | Major: respiratory depression, hypotension and death. |
| • Flexeril (cyclobenzaprine) | Lioresal (baclofen) | |
| • Skelaxin (metaxalone) | Soma (carisoprodol) | |
| **Fioricet (acetaminophen, butalbital, caffeine)** | **Mucinex (guaifenesin)** | Major: respiratory depression, and CNS effects |
| **Sudafed (pseudoephedrine)** | **Muscle Relaxants** | |
| **Anticholinergics** | **Benzodiazepines** | Major: CNS depression, hypotension, and altered alertness |
| • Droperidol | | |
| **Tricyclic Antidepressants** | | |
| • Elavil (amitriptyline) | **Oral Contraceptives** | Decreased plasma concentration of opioids due to induction of conjugation effects |
| **CYP450 inhibitors** | **Antibiotics** | Increased opioid toxicity |
| • Anti-HIV agents | | |
| • Azole antifungals | | |
References

decision-guideline-for-prescribing-opioids-for-chronic-pain—united-states-2016#opioids+guidelines

The Nebraska Council for Continuing Pharmacy Education (NCxCEP) is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education (CPE). This CPE home study activity has been accredited for 1.0 contact hour or 0.1 CEU. UNA 0128-0000-18-018-H05-P for pharmacists and UNA 0128-0000-18-018-H05-T for pharmacy technicians. This is a knowledge-based CPE activity targeted to pharmacists.

The Nebraska Pharmacists Association disclaims any liability to you or your patients resulting from reliance solely upon the information contained herein.

Quiz Answers may be submitted:
Online:  www.npharm.org
Fax:  402-420-1406
Email:  m&p@npharm.org
Mail:  Nebraska Mortar & Pestle 6221 S 58th St, Ste A Lincoln, NE 68516
The Opioid Crisis: Focusing on Drug Interactions

Quiz #5, April 2018, ACPE 0128-0000-18-018-H05-P/T

1. Which of the following is an adverse event that can result from the use of opioid?
   a. Constipation  
b. Diminished testosterone level  
c. Narcotic bowel syndrome  
d. All the above

2. The FDA issued a new warning that recommends against use of codeine and tramadol in children younger than?
   a. 12 years old  
b. 14 years old  
c. 16 years old  
d. 18 years old

3. The FDA added boxed warnings about the combined use to the drug labeling of prescription opioid pain medicines and which of the following drugs?
   a. Benzodiazepines  
b. Chemotherapeutic agents  
c. SSRIs  
d. Tricyclic antidepressants

4. Patients with CYP450 polymorphisms and who are classified as poor metabolizers metabolize drugs at which rate compared to people with normal CYP enzymes?
   a. Faster rate  
b. Intermediate rate  
c. Slower rate  
d. None of the above

5. Which drug(s) are CYP3A4 inhibitors?
   a. Carbamazepine  
b. Darunavir/Ritonavir  
c. Phenobarbital  
d. All the above

6. Which of the following is considered a CYP2D6 inhibitor that decreases the rate of oxycodone metabolism and increases its toxicity?
   a. Dexamethasone  
b. Paroxetine  
c. Phenytoin  
d. None of the above

7. The use of opioids can cause a drug interaction in patients who are on MAOIs or who took MAOIs within the previous______?
   a. 7 days  
b. 14 days  
c. 21 days  
d. 30 days

8. Which drug class(es) can increase the risk for serotonin syndrome if a drug from such class is co-administered with an opioid?
   a. MAOIs  
b. SSRIs  
c. St John’s Wort  
d. All the above

9. Which drug from the following list can increase the risk for CNS depression when co-administered with oxycodone?
   a. Amitriptyline  
b. Ciprofloxacin  
c. Rifampin  
d. Rivaroxaban

10. High plasma concentration of which opioid is associated with QT interval prolongation above 450 ms?
    a. Codeine  
b. Oxycodone  
c. Methadone  
d. Tramadol

Name ____________________________
Mailing Address ____________________________
City/State/Zip ____________________________

Circle one (1) Answer:
1. a b c d  
2. a b c d  
3. a b c d  
4. a b c d  
5. a b c d

CPE Home Study Evaluation
1. Rate this lesson: (Excellent) 5 4 3 2 1 (Poor)
2. Did this lesson meet each of its objectives? ___ Yes ___ No
3. Was the content without commercial bias? ___ Yes ___ No
   If not, please explain_______________________________________
4. Did the lesson meet your educational/practice needs? ___ Yes ___ No
5. Comments/future topics are welcome. _______________________________________

Keep the TOP portion for your records. Return the BOTTOM portion to the NPA office. Or, take this quiz online at www.npharm.org

The deadline for this quiz is December 12, 2018. 
2017 Recipients of the “Bowl of Hygeia” Award

The “Bowl of Hygeia” award program was originally developed by the A. H. Robins Company to recognize pharmacists across the nation for outstanding service to their communities. Selected through their respective professional pharmacy associations, each of these dedicated individuals has made uniquely personal contributions to a strong, healthy community. We offer our congratulations and thanks for their high example. The American Pharmacists Association Foundation, the National Alliance of State Pharmacy Associations and the state pharmacy associations have assumed responsibility for continuing this prestigious recognition program. All former recipients are encouraged to maintain their linkage to the Bowl of Hygeia by emailing current contact information to awards@naspa.us. The Bowl of Hygeia is on display in the APhA History Hall located in Washington, DC.

Boehringer Ingelheim is proud to be the Premier Supporter of the Bowl of Hygeia program.
Amy Friedman Wilson, PharmD’95, has been named interim dean of the Creighton University School of Pharmacy and Health Professions. Wilson, who is currently the associate dean of Academic Affairs in the school, will begin her term in April when current dean J. Chris Bradberry, PharmD, retires.

Wilson graduated from the School of Pharmacy and Health Professions in 1995 and returned to Creighton full-time in 2000 and has since held several leadership roles at the University. For 10 years, she served as the director of the Center for Drug Information and Evidence-Based Practice in the School of Pharmacy and Health Professions. In 2009-2010, she was selected to complete the American Association of Colleges of Pharmacy’s Academic Leadership Fellows Program.

In 2014, in recognition for her work in the School of Pharmacy and Health Professions, and her mentoring of women in pharmacy, she was awarded the Mary Lucretia and Sarah Emily Creighton Award from the University’s Committee on the Status of Women.

“In my roles in the Office of Academic and Student Affairs, I have really enjoyed the opportunity to work with all the programs in our school. I look forward to having more of an opportunity to interface and lead the great work of our school during this time of transition,” says Wilson. “And, as an alumna, I know how important it is to feel connected and I want to be sure that all our alumni feel that connection and realize the valuable role they play in our school.”

“Amy brings a wealth of teaching and clinical service experiences to this position as well as significant administrative experiences as our associate dean for Academic Affairs. Amy will be working with me over the next few months to make her transition as smooth as possible,” says Bradberry. “Our school is in good hands!”

Jenny Tilleman, PharmD’02, has been named president of the Nebraska Pharmacists Association.

Tilleman teaches the Professional Development Seminar Series for the first- through third-year pharmacy students and is a member of the Admissions Committee and the University Athletic Board and chairs the Pharmacy Awards Committee. Tilleman also serves as a preceptor for pharmacy students with several health-related service activities.

Tilleman graduated from the School of Pharmacy and Health Professions in 2002 and then completed a pharmacy practice residency at the Creighton University Medical Center.

She says she enjoys the NPA because she gets to meet and interact with pharmacists across the state and in different practice areas. She says she chose a leadership role in the NPA because as a student, she saw how important it was to be active in professional organizations to advance the profession. “It has been a great learning experience for me to see how we as pharmacists really do have a responsibility to give back to the profession and promote what pharmacists are able to do for our patients,” says Tilleman.

Her goals as NPA president are to improve membership involvement and continue the work of the NPA on the Nebraska MEDs drug disposal program.

Creighton University and Hastings College have forged a new partnership giving Hastings College students priority consideration for admission to the Creighton School of Pharmacy and Health Professions Doctor of Pharmacy program and reduces by one year the time it will take students to earn their degree.

The agreement includes a guaranteed number of slots in both of Creighton’s pharmacy pathways: traditional on-campus instruction in Omaha and a program combining distance learning with shorter on-campus sessions. Enrollment in the program begins with the 2018 incoming class.

“With a growing need for pharmacy practitioners, especially in the rural areas of our state and nation,” says J. Chris Bradberry, PharmD, dean of the School of Pharmacy and Health Professions, “we are pleased to join with Hastings College in extending the Creighton tradition of molding quality, compassionate professionals who are practice ready and eager to serve.”
Nicotine Cessation Counseling:
A Guide for Pharmacists

Objectives
At the conclusion of this lesson, pharmacists should be able to:
1. Devise a plan for nicotine cessation counseling using clinical practice guidelines.
2. Identify common triggers, withdrawal symptoms, and coping techniques for nicotine cessation patients.

Introduction
The Department of Health and Human Services (HHS) published the Healthy People 2020 objectives for tobacco control in the United States. One of the objectives was to reduce the adult cigarette smoking rate to 12 percent or less by the year 2020. Data analyzed from the 2015 National Health Interview Survey found that 15.5 percent of adults (36.5 million people) aged 18 years and over were current smokers.1

High incidences of tobacco-related chronic diseases, losses in productivity, and premature deaths continue to plague the United States. Between 2000-2012, smoking alone resulted in more than $289 billion in annual health-related economic costs including smoking-attributable medical costs and productivity losses.2

According to the Centers for Disease Control and Prevention (CDC), in 2016 more than 2 million middle school and high school students in the United States reported using electronic cigarettes (e-cigarettes) in the past 30 days. More concerning is that among e-cigarette users between the ages of 18 and 24 years, 40% had not been regular cigarette smokers. Electronic cigarettes are also known as e-cigs, e-hookahs, mods, vape pens, vapes, tank systems and electronic nicotine delivery systems (ENDS).3 The risks associated with long-term use of e-cigarettes or vaping are unknown and may vary by product and frequency of use and still expose the user to nicotine.

Tobacco is the leading cause of preventable death and disease in the United States.1 Pharmacists play an integral role in health care prevention and treatment. By developing and implementing a nicotine cessation program, pharmacists may increase quit rates and expand their role in nicotine cessation treatment.

Written and Updated By
Amanda Warren
and Amber Toombs

This continuing pharmacy education lesson was written by Amanda Warren, PharmD, in 2010, and was updated by Amber Toombs, PharmD Candidate, Creighton University School of Pharmacy and Health Professions in 2018. Neither of whom have any conflicts of interest or financial relationships with a commercial interest related to this continuing pharmacy education activity.
Pharmacists should use the information in this article to learn about nicotine cessation and provide useful information to their patients. The article is divided into four counseling sessions. Many cessation programs are designed to target patients who use cigarettes, however, cessation programs can also be used to target patients who smoke, vape or use smoke-less tobacco products. Pharmacists may supplement additional information and other resources to each nicotine cessation session to aid in the success of the program.

Developing a Nicotine Cessation Program Using Clinical Practice Guidelines

The Agency for Healthcare Research and Quality (AHRQ) issued *Treating Tobacco Use and Dependence, a Public Health Service-sponsored Clinical Practice Guideline*. These guidelines are a collaboration of eight Federal Government and nonprofit organizations including the CDC and the National Heart, Lung, and Blood Institute (NHLBI). These guidelines suggest strategies for providing appropriate treatment for patients who use nicotine and recommend that these patients receive at least minimal treatment and counseling every time they visit a pharmacist. The first steps in this process, identification and assessment of nicotine use, separate patients into the three following treatment categories.

(Note - These guidelines were developed prior to the availability of e-cigarettes. A nicotine cessation program should also address patients who would like to quit vaping or using e-cigarettes.)

### Treatment Categories

1. Patients who use nicotine and are willing to quit should be treated using the five A's - ask, advise, assess, assist, and arrange (Table 1).

2. Patients who use nicotine but are unwilling to quit at this time should be treated with the five R's of motivational intervention - relevance, risks, rewards, roadblocks, and repetition (Table 2).

3. Patients who have recently quit using nicotine should be provided relapse-prevention treatment.

Although the above guidelines are suggested for brief intervention for a nicotine user, pharmacists can implement these strategies into their nicotine cessation counseling sessions, making them more suitable for an individual patient’s needs.

The AHRQ expert panel also made important recommendations on the type and intensity of contact with a counselor to the success of the intervention. The following recommendations should be implemented into a nicotine cessation program:

1. There is a strong dose-response relationship between the session length of person-to-person contact and successful treatment outcomes. Intensive interventions are more effective than less intensive intervention and should be used whenever possible. (Strength of Evidence = A). Meta-analysis demonstrated that when interventions last for more than 10 minutes, the increase in cessation rates was better than when interventions did not involve contact with a professional. Contact time with a prescriber for more than 90 minutes, however, did not substantially increase abstinence rates. The number of treatment sessions offered is also important. Providing four or more sessions significantly increased cessation rates, independent of the treatment’s intensity (Strength of Evidence = B).

2. Two types of counseling and behavioral therapies result in higher abstinence rates: (1) providing nicotine users with practical counseling (problem-solving skills/skills training), and (2) providing support and encouragement as part of treatment. These types of counseling elements should be included in nicotine cessation interventions. (Strength of Evidence = B). Group and individual counseling was more effective than no intervention in increasing abstinence rates. Interventions were more successful when they included social support and training in general problem-solving skills, stress management, and relapse prevention.

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Pharmacists who successfully complete this lesson will meet the training requirements necessary to enroll as a Tobacco Cessation Counselor for Nebraska Medicaid.
Table 1 | The “Five A’s” for Brief Intervention

<table>
<thead>
<tr>
<th>Ask about nicotine use.</th>
<th>Identify and document nicotine use status for every patient at every visit.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advise to quit.</td>
<td>In a clear, strong and personalized manner urge every nicotine user to quit.</td>
</tr>
<tr>
<td>Assess willingness to make a quit attempt.</td>
<td>Is the nicotine user willing to make a quit attempt at this time?</td>
</tr>
<tr>
<td>Assist in quit attempt.</td>
<td>For the patient willing to make a quit attempt, use counseling and pharmacotherapy to help him or her quit.</td>
</tr>
<tr>
<td>Arrange follow-up.</td>
<td>Schedule follow-up contact, preferably within the first week after the quit date.</td>
</tr>
</tbody>
</table>

Table 2 | The “Five R’s” for Enhancing Motivation to Quit Nicotine

<table>
<thead>
<tr>
<th>Relevance</th>
<th>Encourage the patient to indicate why quitting is personally relevant, being as specific as possible. Motivational information has the greatest impact if it is relevant to a patient’s disease status or risk, family or social situation (e.g. having children in the home), health concerns, age, gender, and other important patient characteristics (e.g. prior quitting experience, personal barriers to cessation).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks</td>
<td>The pharmacist should ask the patient to identify potential negative consequences of nicotine use. Suggest and highlight those that seem most relevant to the patient. The pharmacist should emphasize that smoking low-tar/low-nicotine cigarettes or use of the other forms of nicotine (e.g. smokeless tobacco, e-cigarettes, vaping, cigars, and pipes) will not eliminate these risks.</td>
</tr>
<tr>
<td>Rewards</td>
<td>Ask the patient to identify potential benefits of stopping nicotine use. The pharmacist may suggest and highlight those benefits that seem most relevant to the patient.</td>
</tr>
<tr>
<td>Roadblocks</td>
<td>The pharmacist should ask the patient to identify barriers or impediments to quitting and note elements of treatment (problem solving, pharmacotherapy) that could address barriers.</td>
</tr>
<tr>
<td>Repetition</td>
<td>The motivational intervention should be repeated every time an unmotivated patient visits the pharmacy. Nicotine users who have failed in previous quit attempts should be told that most people make repeated quit attempts before they are successful.</td>
</tr>
</tbody>
</table>

3. The combination of counseling and medication is more effective for nicotine cessation than either medication or counseling alone. Therefore, whenever feasible and appropriate, both counseling and medication should be provided to patients trying to quit using nicotine. (Strength of Evidence = A).

First Counseling Session: Getting to Know the Patient

The Introduction
Establishing a strong relationship between the pharmacist and patient at the initial meeting is important. The patient should feel comfortable and be able to express his or her thoughts and feelings without embarrassment or shame. This will make treatment, both physical and psychological, more efficacious and less problematic. The pharmacist should be informative, compassionate, an active listener, and able to communicate to the patient in a language that is clear and understandable. The pharmacist should begin by introducing himself or herself and stating the purpose of the nicotine cessation counseling sessions. The intent of these sessions is to aid the patient in preparing to quit and remaining abstinent from using nicotine, providing the patient understanding about nicotine addiction, finding a suitable pharmacological treatment option, providing coping mechanisms for nicotine withdrawal, identifying and avoiding triggers, and providing the patient with useful nicotine cessation resources.

It is also important for patients to understand that successfully quitting nicotine is not an overnight process. It takes time, commitment, and planning to become completely nicotine-free. By reassuring the patient that, with the right tools, medication, and support provided by these meetings, the likelihood of maintaining nicotine-free lifestyle is possible.

Assessing Past Medical History of the Patient
The next step is to assess the patient by gathering background information and past medical history. Based on this information, the pharmacist can make informed recommendations to the patient’s primary care provider and select an appropriate nicotine cessation medication. The pharmacist should obtain the patient’s name, contact information, date of birth, gender, ethnicity, and vital signs (blood pressure, pulse and weight). The pharmacist should ask about allergies to any medications, comorbid conditions, and past surgical history.
Family history of disease states such as diabetes mellitus or coronary heart disease is important to know as well. This information can be used to motivate the patient to stay abstinent and avoid potential health problems that can be exacerbated by nicotine use. If the patient is female, the pharmacist should ask if she is taking any contraceptives, is pregnant, or plans on becoming pregnant. Safe pharmacotherapy treatments are limited in women of childbearing potential. Other populations that may need extra consideration are nicotine users with psychiatric comorbidity and/or additional chemical dependencies, and adolescent nicotine users. Nicotine cessation may increase plasma levels of some drugs to potentially toxic levels. Abstinence from smoking reverses smoking-induced CYP1A2 hepatic enzyme levels to normal, increasing plasma concentrations in patients whose dose was established while smoking. Certain medications are affected by tobacco smoke through pharmacokinetic (PK) or pharmacodynamic (PD) mechanisms. PK interactions affect the absorption, distribution, metabolism, or elimination of other drugs which can potentially cause an altered pharmacologic response. PD interactions alter the expected response or actions of other drugs; therefore, a detailed list of current medications, prescribed and over-the-counter, should be obtained. Pharmacists should carefully review the dosage form, strength, and regimen of each drug and adjust or monitor those that are affected by smoking cessation. See Table 3 for a list of some drugs affected by smoking cessation and dose adjustments after cessation. Table 3 is not a complete list of all drugs that are affected by nicotine use.

Assessing Nicotine Use History of the Patient

There are a variety of questionnaires available to assess nicotine use status. The pharmacist may choose to use a questionnaire provided by a smoking cessation organization or create a customized evaluation. Regardless of which tool is utilized, the information gathered by the survey should be used to appropriately evaluate behavior and nicotine dependence. The following questions should be asked of every patient starting the nicotine cessation program:

1. What age did the patient start using nicotine? How many years?
2. Why did the patient start using nicotine?
3. How much nicotine does the patient use daily (e.g., number of cigarettes or the number of cans/pouches)?
4. When does the patient smoke/use nicotine?
5. What kinds of activities or “triggers” increase the urge to use nicotine?

The Fagerström Test for Nicotine Dependence (FTND) is a standard instrument for assessing the intensity of physical addiction to nicotine. This self-survey can provide some insight concerning behavior and addiction in addition to using other evaluation tools. The higher the score on the Fagerström Test, the more physically dependent the patient is to nicotine. Higher scoring patients may need additional counseling and more intense medication treatment(s) to successfully quit nicotine than lower scoring patients. See Table 4 for the Fagerström Test for smoking tobacco. This questionnaire can be modified for those patients who use smokeless-tobacco.

Assessing Past Quit Attempts

To some patients, talking about past quit attempts can be frustrating. The average smoker tries to quit 6 to 9 times in a lifetime. The patient has probably tried to stop using nicotine independently without talking to a health care professional. Seeking help from a smoking cessation counselor could be a last resort for some smokers who have tried numerous times to quit, but have not been successful. This topic can be a source of shame and embarrassment. Past quit attempts are important to discuss with the patient. It is an initial starting point in figuring out which medications and behavior modifications worked well in the past and what did not. Every patient should be asked the following questions:

1. Has the patient attempted to quit using nicotine before? How many times?
2. How long did the patient stay nicotine-free?
3. Which nicotine cessation product(s) did they use before?
4. Which product(s) worked well for the patient? Which didn’t?
5. Did the patient modify any behaviors/change routines while staying nicotine-free?
6. Why did the patient start using nicotine again?

Determining the Patient’s Readiness to Quit

Understanding the patient’s readiness to quit may lead to a more efficient and productive conversations during meetings. Each patient will be at different stages of the quitting process. Some patients may need more motivation than others. Those that are less ready to quit may need to be reminded of the health benefits and financial savings associated with nicotine cessation. With those that are highly motivated, the pharmacist may want to focus more time on developing a plan to quit smoking. Table 5 is a patient self-survey designed to help assess readiness to quit. It is based on information gathered from a national study involving both smokers and recent quitters and developed to identify motivation to quit smoking. This survey can be modified for patients who use smokeless tobacco. The higher the score on the survey, the more ready the patient is to quit nicotine.
## Table 3 | Drug Interactions with Smoking

### Pharmacokinetic Interactions

<table>
<thead>
<tr>
<th>Drug/Class</th>
<th>Effects After Cessation</th>
</tr>
</thead>
<tbody>
<tr>
<td>alprazolam</td>
<td>Conflicting data on significance of a PK interaction; Possible ↓ in plasma concentrations and half-life.</td>
</tr>
<tr>
<td>caffeine</td>
<td>↑ clearance and ↓ serum concentrations; ↓ use after cessation.</td>
</tr>
<tr>
<td>chlorpromazine</td>
<td>↑ clearance and ↓ serum concentrations; Monitor carefully when changes in smoking status occur.</td>
</tr>
<tr>
<td>flecainide</td>
<td>↑ clearance and ↓ serum concentrations; Clinicians should be aware of the possibility of an interaction, but no specific dosage adjustment parameters are recommended.</td>
</tr>
<tr>
<td>fluvoxamine</td>
<td>Smokers have a 25% ↑ in metabolism over non-smokers; ↓ clearance and ↑ serum concentrations; Monitor for the desired clinical effects when changes in smoking status occur.</td>
</tr>
<tr>
<td>haloperidol</td>
<td>↑ clearance and ↓ serum concentrations; Monitor patients carefully when changes in smoking status occur.</td>
</tr>
<tr>
<td>heparin</td>
<td>Mechanism unknown but ↑ clearance and ↓ half-life has been observed with smokers; Smoking has prothrombotic effects; Smokers may need increased dosages.</td>
</tr>
<tr>
<td>insulin</td>
<td>Cessation may result in ↓ blood glucose or ↑ the subcutaneous absorption of insulin. Monitor for the desired clinical effects when changes in smoking status occur.</td>
</tr>
<tr>
<td>mexiletine</td>
<td>↑ clearance and ↓ serum concentrations; Monitor for desired clinical effects when changes in smoking status occur.</td>
</tr>
<tr>
<td>olanzapine</td>
<td>Following one week of abstinence from chronic tobacco smoking, clearance may ↓; Monitored carefully when changes in smoking status occur.</td>
</tr>
<tr>
<td>propranolol</td>
<td>↑ clearance and ↓ serum concentrations; No specific dosage adjustments are recommended; Monitor carefully for the desired clinical effects when changes in tobacco smoking status occur.</td>
</tr>
<tr>
<td>tacrine</td>
<td>↑ clearance and ↓ serum concentrations; Monitor for desired clinical effects when changes in smoking status occur.</td>
</tr>
<tr>
<td>theophylline</td>
<td>Following one week of abstinence from chronic tobacco smoking, clearance may ↓ by roughly 40%, leading to ↑ in serum concentrations. Theophylline serum concentrations should be monitored carefully when changes in smoking status occur.</td>
</tr>
<tr>
<td>tricyclic antidepressants</td>
<td>Possible interaction; ↓ serum concentrations, but clinical importance is not established.</td>
</tr>
<tr>
<td>warfarin</td>
<td>↑ clearance; this may not result in a clinically significant change in the PT or INR; Monitor patient’s INR to assess the need for warfarin dosage adjustment when changes in smoking status occur.</td>
</tr>
</tbody>
</table>

### Pharmacodynamic Interactions

<table>
<thead>
<tr>
<th>Drug /Class</th>
<th>Effects of Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines (diazepam, chlordiazepoxide)</td>
<td>↑ metabolism of major metabolite by up to three-fold. No specific dosage adjustment recommendations are available but monitor patients for the desired clinical effects when changes in tobacco smoking status occur.</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>↑ clearance and ↓ serum concentrations after cessation; Blood pressure, angina and exercise tolerance are improved less by beta-blocker therapy when the patient is a smoker than when not smoking; Monitor carefully for the desired clinical effects when changes in tobacco smoking status occur.</td>
</tr>
<tr>
<td>Corticosteroids, inhaled</td>
<td>Asthmatic smokers may have less of a response to inhaled corticosteroids.</td>
</tr>
<tr>
<td>Hormonal contraceptives</td>
<td>↑ risk of cardiovascular adverse effects (e.g. stroke, myocardial infarction, thromboembolism) in women who smoke and use oral contraceptives; Risk is especially high for women age 35 or older or those who smoke 15 cigarettes or more per day.</td>
</tr>
<tr>
<td>Opioids (propoxyphene, pentazocine)</td>
<td>↑ in the therapeutic effects as hepatic enzyme activities return to normal after cessation.</td>
</tr>
</tbody>
</table>
Table 4  | Fagerström Test for Nicotine Dependence\textsuperscript{a}

<table>
<thead>
<tr>
<th>Questions</th>
<th>Answers</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>How soon after you wake up do you smoke your first cigarette?</td>
<td>Within 5 minutes</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>6 to 30 minutes</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>31 to 60 minutes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>After 60 minutes</td>
<td>0</td>
</tr>
<tr>
<td>Do you find it difficult to refrain from smoking in places where it is</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>forbidden such as in church, the library, or movie theaters?</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Which cigarette would you most hate to give up?</td>
<td>The first one in the morning</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>All others</td>
<td>0</td>
</tr>
<tr>
<td>How many cigarettes/day do you smoke?</td>
<td>10 or fewer</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>11 to 20</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>21 to 30</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>31 or more</td>
<td>3</td>
</tr>
<tr>
<td>Do you smoke more frequently during the first hours after waking than</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>during the rest of the day?</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Do you smoke when you are so ill that you are in bed most of the day?</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
</tr>
</tbody>
</table>

Score: 0-2 very low addiction; 3-4 low addiction; 5 medium addiction; 6-7 high addiction; 8-10 very high addiction

**Identifying Personal Goals for Staying Smoke-Free**

The pharmacist should ask every patient this important question, “why do you want to quit?” Having patients give a reason for quitting nicotine use will give them accountability for their actions. The patient is responsible, not only for setting personal goals, but also for implementing a plan to achieve them. The pharmacist can provide helpful tools for the patient to succeed. Patients should have constant reminders of their goals. For example, the patient could write his/her personal goal(s) on every handout received during cessation meetings. This can keep patients focused on staying nicotine-free.

When it comes to actually quitting nicotine use, some people may find it hard to plan ahead and prepare for relapse or difficult situations. Giving a step-wise action plan to the patient is a good solution. In the action plan, patients should list their long-term goals, short-term goals, how to achieve these goals, what obstacles or roadblocks might be encountered and how to overcome them, and what rewards can be given for successfully achieving each goal. The pharmacist should remind the patient to take the time to thoughtfully write out an answer to each topic and bring the responses back to the next meeting for review.

**Keeping a Nicotine Use Log**

The patient should be instructed to document his or her nicotine use for the next several days. This information can provide a clearer overall picture of the patient’s addiction to nicotine. Writing down every time the patient uses nicotine can help to identify which emotional states and activities trigger the urge to use nicotine throughout the day. With each use, the patient should write down the following information: the date and time, the location, the activity the patient is doing while smoking, the patient’s current mood, and the strength of the craving for the nicotine product. A simple nicotine log sheet can be created by the pharmacist and provided to the patient. The pharmacist should instruct the patient to continue his or her normal daily routines while documenting use. The information gathered will be discussed at the next nicotine cessation meeting.

**Selecting the Right Medication and Quit Date**

It is ultimately the patient’s decision to start a nicotine cessation medication. While it is possible to quit nicotine “cold turkey”, the success rate of staying abstinent is approximately doubled with the use of pharmacotherapies.\textsuperscript{3} With many products available for treatment of nicotine dependence, this can be overwhelming for the patient. The pharmacist can aid in the selection of an appropriate therapy based on the patient’s past medical history and past quit attempts. A patient-oriented medication guide listing the advantages and disadvantages of each drug should be provided to
Table 5 | Ready to Quit Survey\textsuperscript{2}

<table>
<thead>
<tr>
<th>Questions</th>
<th>Answers</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>I want to quit smoking for my own personal reasons, not because I feel pressured to quit by others.</td>
<td>Completely Disagree</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Somewhat Disagree</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Somewhat Agree</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Completely Agree</td>
<td>5</td>
</tr>
<tr>
<td>I have a specific plan in mind to try to quit smoking.</td>
<td>Completely Disagree</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Somewhat Disagree</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Somewhat Agree</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Completely Agree</td>
<td>5</td>
</tr>
<tr>
<td>I am always looking for new ways to help me not smoke.</td>
<td>Completely Disagree</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Somewhat Disagree</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Somewhat Agree</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Completely Agree</td>
<td>5</td>
</tr>
<tr>
<td>I want to quit smoking because I worry a lot about how smoking affects my health.</td>
<td>Completely Disagree</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Somewhat Disagree</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Somewhat Agree</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Completely Agree</td>
<td>5</td>
</tr>
<tr>
<td>I want to quit smoking because I am tired of being a prisoner to my cigarettes.</td>
<td>Completely Disagree</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Somewhat Disagree</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Somewhat Agree</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Completely Agree</td>
<td>5</td>
</tr>
</tbody>
</table>

Scale 5 - 25 Less ready to quit (lower score); More ready to quit (higher score)

March/April 2018

the patient. The pharmacist should instruct the patient to review the medication guide, write down any additional questions about each drug, and select a drug(s) that he or she would prefer to use. It is important to remind the patient that there are two parts to nicotine addiction, a physical and a behavioral component, and that medications only treat the physical addiction.\textsuperscript{14} Combination therapy of both medication and counseling can significantly improve abstinence rates.\textsuperscript{5}

The quit date should also be determined by the patient. The pharmacist should instruct the patient to take the time to select a day in the near future. Initially, it may take a lot of concentration and focus to stay abstinent. Therefore, the actual quit date should not be scheduled on a highly stressful day such as an upcoming wedding, graduation, or traumatic event in the patient's life. The patient should write the quit date on a calendar and then share the date with family and friends. Support from family and friends may help the patient stick to the goal of staying smoke-free. Table 6 provides a quick summary to patients on how to quit using nicotine and can be given as an additional motivational guide.

Second Meeting: Preparing for the Quit Date
Assessing the Nicotine Use Log
After the patient has had time to process and complete the information provided in the first nicotine cessation meeting, it is time to assess the patient’s nicotine use log. The patient has documented his or her nicotine use for at least the last three to four days and has set a quit date. The nicotine use log can be discussed before, during, or after the pharmacist has presented to the patient the new material for the second cessation meeting. The pharmacist should relate the new information to help solve
the patient’s current nicotine use problems and aid in the preparation of the upcoming quit date. By the end of the second meeting, the pharmacist should address why it is hard to quit nicotine, the symptoms of nicotine withdrawal, the triggers are and how to manage them, the difference between a slip and a relapse, and other nicotine cessation resources.

### Addressing the Physical and Psychological Addiction to Nicotine

For a successful recovery from nicotine use, patients should understand how nicotine affects the brain and why it can be difficult to quit using nicotine. A patient-oriented handout about the physical and psychological effects of nicotine should be given to the patient to aid in what to expect when quitting nicotine.

Nicotine is a highly addictive, potent, and psychoactive drug. A single cigarette typically delivers between 1.2-3.2 mg of nicotine, while other nicotine products can deliver many times that amount. The absorption rate of nicotine from the lungs is rapid, producing with each inhalation a high concentration arterial bolus of nicotine which reaches the brain within 15 seconds, faster than by intravenous injection. The elimination half-life of nicotine lasts for about two hours. Because the brain is a highly perfused organ, nicotine will quickly redistribute into plasma to achieve equilibrium in the body. As a result, the effective half-life of nicotine on dopamine receptors is shorter than its elimination half-life. The quick onset and short half-life of nicotine frequently leads to repeated administration to maintain raised concentrations in the brain.

Nicotine produces a wide range of central nervous system, cardiovascular, and metabolic effects. It activates nicotinic acetylcholine receptors (nAChRs) in the brain and induces the release of dopamine in the nucleus accumbens, the reward center of the brain. This effect is the same as that produced by other addictive drugs such as amphetamines and cocaine and is thought to be a critical component in brain addiction mechanisms. The activation of the dopamine reward pathway gives the user a feeling of pleasure. Nicotine also causes other psychological effects such as cognitive enhancement, mood modulation, and reduction of anxiety and tension. Between administrations of nicotine, the level of dopamine declines and the nicotine user starts to experience withdrawal symptoms such as irritability and stress. The brain craves nicotine to release more dopamine to bring it back to a level of pleasure and calm.

Over time, nicotine users develop tolerance to the effects of nicotine. Nicotine users learn to titrate their nicotine levels throughout the day to avoid withdrawal symptoms, to maintain pleasure and arousal, and to modulate their mood. This typically leads to strong, repetitive habits, and behavior rituals associated with nicotine use. For example, smokers often smoke at certain times of the day, during certain activities, in certain locations, after a meal, or under certain levels of stress.

<table>
<thead>
<tr>
<th>Table 6</th>
<th>Steps on How to Quit&lt;sup&gt;15&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Pick your quit date.</td>
</tr>
<tr>
<td>2.</td>
<td>Decide how you want to quit: using medication and gradually cutting back or quitting all at once.</td>
</tr>
<tr>
<td>3.</td>
<td>Throw it away! Throw away everything related to nicotine use including cigarettes, ashtrays, lighters, and matches.</td>
</tr>
<tr>
<td>4.</td>
<td>Get support. Start to build a support network (family and friends) and keep them updated and involved with your progress.</td>
</tr>
<tr>
<td>5.</td>
<td>After quit date arrives, don’t use nicotine. If you do have a slip, recommit to quitting right away. Remember your long-term goals and the rewards for not using nicotine (health, financial, family).</td>
</tr>
<tr>
<td>6.</td>
<td>Track your progress. Keep a record of your progress. Note any questions you may want to ask for the next meeting.</td>
</tr>
<tr>
<td>7.</td>
<td>Remember to keep trying!</td>
</tr>
</tbody>
</table>
**Recognizing Nicotine Withdrawal Symptoms**

Patients who have used nicotine on a regular basis will experience nicotine withdrawal symptoms if they suddenly quit using all nicotine products or if they greatly reduce their nicotine use. Because of the short half-life of nicotine, the urge to use nicotine may occur within hours of the last use. Symptoms peak about 2 to 3 days later when nicotine and its metabolites are eliminated from the body. Symptoms of withdrawal, however, may last for a few days or weeks. Knowing what to expect and understanding that withdrawal symptoms gradually decrease with time can help the patient stay abstinent. Although symptoms may be different for each patient, common signs of nicotine withdrawal include anxiety; craving for nicotine; decreased blood pressure and heart rate; depression; difficulty concentrating; drowsiness; frustration, irritability, impatience; gastrointestinal disturbances; headache; hostility; increase in appetite and weight gain; increased skin temperature; insomnia; and restlessness. A list with these common signs can be a useful tool for the patient. The pharmacist can also encourage the patient to think of these withdrawal symptoms as a positive process in which his or her body is ridding itself of nicotine.

**Identifying Triggers and Coping Techniques**

Repetitive habits and behavior rituals associated with nicotine use eventually are incorporated into the nicotine addiction. These behavior rituals are closely coupled with sensory aspects of nicotine use. For example, for a patient who smokes, each puff of nicotine delivered to the brain is linked to the sight of the pack and the smell of the smoke. The activity that the patient is doing at the time becomes the reason to use nicotine. The reward of smoking is associated with the activity. This accounts for smokers’ widespread concern that if they stopped smoking they would not know what to do with their hands, and for the ability of smoking-related cues or “trigger” to evoke strong cravings.

Treatment for the psychological addiction to nicotine is accomplished by breaking triggers through behavior modification. This is done by modifying the patient’s behaviors, changing routines, and learning how to deal with stressful issues without using nicotine as a coping mechanism.

**Table 7 | Common Triggers and How to Manage Them**

<table>
<thead>
<tr>
<th>Triggers</th>
<th>Suggested Coping Techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Being around others who smoke.</td>
<td>Go to places where smoking isn’t allowed. Tell friends who smoke you are trying to quit.</td>
</tr>
<tr>
<td>Feeling bored.</td>
<td>Find new ways to occupy your time. Read, walk, start a new hobby.</td>
</tr>
<tr>
<td>Drinking alcohol.</td>
<td>Avoid alcohol while you are trying to stop smoking.</td>
</tr>
<tr>
<td>Feeling hungry.</td>
<td>Have a healthy snack or drink water. Exercise can also help.</td>
</tr>
<tr>
<td>Drinking coffee.</td>
<td>Switch to tea, or hold your cup in the hand you used to hold your cigarette in.</td>
</tr>
<tr>
<td>Talking on the telephone.</td>
<td>Put something else in your hand, like a pen, straw, doodle on a scratch pad.</td>
</tr>
<tr>
<td>Watching television.</td>
<td>Do not sit in your usual chair. Keep popcorn or low-fat healthy snacks on hand.</td>
</tr>
<tr>
<td>Finishing a meal.</td>
<td>Brush your teeth after eating. Take a walk.</td>
</tr>
<tr>
<td>Feel nervous, stressed, or anxious.</td>
<td>Try relaxation techniques.</td>
</tr>
<tr>
<td>Waking up in the morning.</td>
<td>Usually the <strong>toughest</strong> time for smokers. Take a shower, eat breakfast, exercise, or brush your teeth as soon as you get up. <strong>CHANGE</strong> your routine.</td>
</tr>
<tr>
<td>Driving to and from work.</td>
<td>Play music, take a different route, carpool with a nonsmoker, or walk to work if possible. Spend the money to detail your car before your quit day so you will not be tempted by the smell of tobacco.</td>
</tr>
</tbody>
</table>

Table 7 provides some examples of common triggers and ways to avoid them. This table can be modified for patients who use smokeless tobacco.

Based on the patient’s comments on the nicotine log and past smoking history, the pharmacist should have the patient complete a trigger log which identifies the patient’s own triggers and how the patient will manage them. This log should be displayed somewhere visible so that the patient will be reminded of what to do when the trigger occurs.
One of the most difficult times to avoid using nicotine is when the patient wakes up in the morning. During the night, the patient has become deprived of nicotine. Nicotine blood concentration levels drop close to those of non-smokers. The first cigarette or other nicotine product releases dopamine in the brain and gives the patient a strong sense of pleasure and calmness. The pharmacist should advise patients to change their morning routines to avoid the urge to use nicotine.

The pharmacist can also provide patients a list of activities to do instead of smoking which may help patients occupy their time and stay focused on their long-term goals. Suggested activities could include starting a new hobby, going to the movies, library, or a bookstore, doing some spring cleaning around the house, chewing sugarless gum, drinking water, or starting an exercise program.

Understanding the Difference between a Slip and a Relapse
Quitting nicotine permanently can be challenging for many nicotine users. Few people never slip at all. Turning a slip into a relapse is under the control of the patient. It is important for the pharmacist to explain what the difference is between a slip and a relapse. A slip is a one-time mistake that is quickly corrected while a relapse is going back to using nicotine. A slip is not a failure. The patient can still successfully quit. If the patient uses nicotine, he or she should stop using again right away and recommit to quitting. The pharmacist should ask the patient to write down the reason(s) for the slip and what he or she could have done differently. The pharmacist should encourage the patient not to become disappointed. The patient can use this information to make a stronger attempt at quitting the next time the troubling situation occurs.

Providing Additional Nicotine Cessation Resources to the Patient
There are many nicotine cessation resources available through professional organizations, federal or state funded quitting programs, and websites. Pharmacists have access to vast amounts of useful information, which provided to the patient, can help further understanding about nicotine cessation. Selecting the right information to meet an individual patient’s needs can be challenging. Each counseling session is unique and specific to each patient. Patients will be at different stages of the quitting process. This could be the first or the last attempt at quitting nicotine. Some patients will be more motivated to try anything new, while others will need more encouragement and guidance. Also, each patient’s comprehension level for understanding and processing information will be different. Therefore, it is important that additional resources provided by the pharmacist are not only customized to address the patient’s current situation, but also written in a language that the patient will understand.

Third Meeting: Follow-up After the Quit Date Addressing the Patient’s Concerns
The next meeting with the patient should take place after the patient’s quit date. The patient should be refraining from using nicotine for some time and should be taking the prescribed medication(s). This meeting should address the patient’s concerns and provide the patient with more motivation to stay abstinent from nicotine. This meeting should also be used to answer the patient’s questions about the medication(s) he or she is currently taking, any triggers or slips that he or she has experienced since the quit date, and any additional roadblocks that are preventing the patient from staying nicotine-free. The pharmacist can suggest ways to manage difficult triggers and review the material presented from previous meetings. It is also important that the pharmacist review the difference between a slip and a relapse. Successfully quitting nicotine takes commitment, concentration, planning, and time.

Understanding the Health Risks Associated with Continued Nicotine Use
In the United States, tobacco use is responsible for nearly 1 in 5 deaths. As a result of smoking or exposure to secondhand smoke, more than 440,000 premature deaths and 5.1 million years of potential life was lost each year between 2000-2004. During that period, smoking-attributable health care expenditures totaled an estimated $100 billion annually, up $24 billion from $75.5 billion spent during 1999-2001.

Cigarette smoking substantially increases the risk of cardiovascular diseases such as stroke, sudden death, and heart attack; nonmalignant respiratory diseases including emphysema, asthma, chronic bronchitis, and chronic obstructive pulmonary disease; lung cancer; and other cancers such as mouth, pharynx, larynx, esophagus, stomach, pancreas, uterus, cervix, kidney, ureter, and bladder. The risk of developing lung cancer is about 23 times higher in male smokers and 13 times higher in female smokers compared to lifelong nonsmokers. Smokeless tobacco users have a four-fold greater risk of oral cancer than nonusers. The risk increases up to 50-fold for long term users. Half of all those who continue to smoke will die from smoking-related diseases.

Exposure to environmental tobacco smoke (i.e. secondhand smoke) has been cited as the cause of 3,400 lung cancer deaths and 46,000 heart disease deaths in nonsmoking adults in the United States every year.
exposed to environmental smoke have a higher risk of respiratory infection, asthma, and middle ear infections than those who are not exposed. Sudden infant death syndrome (SIDS) occurs more often in infants whose mothers smoked during pregnancy than in offspring of nonsmoking mothers. Smoking during pregnancy also reduces fetal growth and increases the risk of ectopic pregnancy and spontaneous abortion.

A pharmacist should discuss with their patients the health consequences associated with continued nicotine use and how they can be prevented by nicotine cessation. From the AHRQ guidelines, Table 8 summarizes some of the health risks related to nicotine use.

### Understanding the Rewards of Staying Nicotine-free

The patient may need more motivation to resist the temptation of using nicotine again. Table 9 from the AHRQ guidelines provides other examples of rewards for staying nicotine-free. Aside from decreasing morbidity and mortality, patients can also save money when they quit nicotine.

<table>
<thead>
<tr>
<th>Risks</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>Shortness of breath, exacerbation of asthma, harm to pregnancy, infertility, increased serum carbon monoxide.</td>
</tr>
<tr>
<td>Long-term</td>
<td>Heart attacks and strokes, lung and other cancers (larynx, oral cavity, pharynx, esophagus, pancreas, bladder, cervix), chronic obstructive pulmonary disease (chronic bronchitis and emphysema), long-term disability and need for extended care.</td>
</tr>
<tr>
<td>Environmental</td>
<td>Increase risk of lung cancer and heart disease in spouses; higher rates of smoking by children of tobacco users; increase risk for low birth weight, SIDS, asthma, middle ear disease and respiratory infections in children of smokers.</td>
</tr>
</tbody>
</table>

The pharmacist can provide the patient a nicotine cost calculator and examples of items that can be bought with the potential money saved by quitting nicotine. The average retail price of a pack of 20 cigarettes (full-priced brands), including federal and state excise taxes, varied by state, ranging from $5.12 in Missouri to a high of $10.66 in New York, as of November 2016. For a pack-a-day smoker, by not buying cigarettes the patient could save enough money to purchase: an iPad (worth approximately $300) in under two months; a flat-screen television (worth $900) in only six months; or a four-day cruise for two people (worth over $1,800) in one year.

In addition to improving health and saving money, the patient can also spend more time doing something more enjoyable or productive. The pharmacist can help the patient figure out how much time is saved. On average the smoking time for one cigarette is five minutes.

By multiplying this number with how many cigarettes the patient smokes per day, the patient can calculate how many minutes are gained per day, month, or year.

The pharmacist can then encourage the patient to write down and think about what he or she can do with the money saved and the time gained from not using nicotine. For example, the patient could start a new hobby which could help with avoiding triggers and nicotine use.

### Fourth Meeting: Maintaining Abstinence from Nicotine Use

#### Addressing Roadblocks and How to Overcome Them

The final meeting with the patient should be reserved to address any concerns from the previous nicotine cessation sessions. The pharmacist should evaluate the patient’s current progress and address any additional problems or roadblocks that are still interfering with complete nicotine cessation. The pharmacist should also review any important topics from previous meetings which will help keep the patient motivated.

The patient should be reminded to stay focused on the long-term goal, to utilize any handouts or resources that have been provided, and to remember his or her reasons for quitting. Table 10 provides common roadblocks encountered by patients and possible actions that clinicians can take to solve the problem.
Table 10  | Addressing Problems Encountered by Former Smokers

<table>
<thead>
<tr>
<th>Problems</th>
<th>Responses</th>
</tr>
</thead>
</table>
| Lack of support for cessation               | • Schedule follow-up visits or telephone calls with the patient.  
• Urge the patient to call the national quit line network (1-800-QUIT-NOW) or other local quit line.  
• Help the patient identify sources of support within his or her environment.  
• Refer the patient to an appropriate organization that offers cessation counseling or support. |
| Negative mood or depression                 | • If significant, provide counseling, prescribe appropriate medications, or refer the patient to a specialist.                                                                                             |
| Strong or prolonged withdrawal symptoms     | • If the patient reports prolonged craving or other withdrawal symptoms, consider extending the use of an approved pharmacotherapy or adding/combining pharmacologic medications to reduce strong withdrawal symptoms. |
| Weight gain                                 | • Recommend starting or increasing physical activity.  
• Reassure the patient that some weight gain after quitting is common and usually is self-limiting.  
• Emphasize the health benefits of quitting relative to the health risks of modest weight gain.  
• Suggest low-calorie substitutes such as sugarless chewing gum, vegetables, or mints.  
• Maintain the patient on medication known to delay weight gain (e.g. bupropion SR, Nicotine Replacement Therapies – particularly 4 mg nicotine gum and lozenge).  
• Refer the patient to a nutritional counselor or program. |
| Smoking lapses                              | • Suggest continued use of medications, which can reduce the likelihood that a lapse will lead to a full relapse.  
• Encourage another quit attempt or a recommitment to total abstinence.  
• Reassure that quitting may take multiple attempts and use the lapse as a learning experience.  
• Provide or refer for intensive counseling. |

Completing and Evaluating the Nicotine Cessation Program

Congratulations should be offered to the patient for completing the nicotine cessation program. Patients should feel a sense of pride for the effort and commitment that they have shown to become nicotine-free. Patients should also reflect on the last four sessions as a learning experience and should use the information daily. At the end of the meeting, the pharmacist can provide the patient a certificate of achievement. This certificate can recognize the patient’s dedication to quitting nicotine and hope for further success, and a longer, healthier, and nicotine-free life. Part of this meeting should consist of a patient evaluation about the nicotine cessation program. The pharmacist should explain that completing the questionnaire will help make improvements to the program so that future patients can benefit. Questions listed on the survey should include the following:

1. How would you describe your health before you quit nicotine?
2. How would you describe your health now after you quit nicotine?
3. What activities do you think were helpful in quitting nicotine?
4. What activities do you think were not helpful in quitting nicotine?
5. What was the hardest nicotine trigger to manage/overcome?
6. What advice will you take with you from completing this program?
7. What advice would you give to other nicotine users trying to quit?
Conclusion

Pharmacists understand the pathophysiology and pharmacotherapy involved in the treatment and recovery from nicotine addiction. With this knowledge, pharmacists can guide patients in preparing to quit and remaining abstinent from using nicotine, finding a suitable pharmacological treatment option, providing coping mechanisms for nicotine withdrawal, identifying and avoiding triggers, and providing useful nicotine cessation resources.

Using the right tools and resources, pharmacists can develop and implement a successful nicotine cessation program, increasing quit rates and expanding the pharmacist’s role in nicotine treatment. With more nicotine cessation programs, the government’s objective to further reduce the adult nicotine use rates, which prevents premature deaths and reduces health care costs, may become a reality.

References

14. Klingemann J. Redefining “cold turkey”: a new way of looking at an old method. PowerPoint presentation presented at: Olson Center for Women’s Health; May 20, 2008; Omaha, NE.
21. Rx for change

Quiz Answers may be submitted:

Online: www.npharm.org
Fax: 402-420-1406
Email: m&p@npharm.org
Mail: Nebraska Mortar & Pestle 6221 S 58th St, Ste A Lincoln, NE 68516

Policies for the Nebraska Mortar & Pestle (M&P) continuing pharmacy education lessons and quizzes:

1. M&P Quizzes are valid only for the membership year in which they are published. Quizzes for the 2018 Membership Year must be received by December 12, 2018. Quizzes cannot be carried over to another membership year.
2. If more than three questions are missed, the quiz will be returned. The quiz can be resubmitted.
3. CPE transcripts can be printed from NABP e-Profiles at www.nabp.net.
4. CPE credits are submitted to NABP by the 15th of each month. For example, M&P CPE quizzes completed in the month of June 2018 will be sent to NABP e-Profiles before July 15, 2018.
Nicotine Cessation Counseling: A Guide for Pharmacists

1. Which of the following statements is true regarding nicotine cessation counseling?
   a. Patients who have quit using nicotine recently should not be provided relapse prevention treatment.
   b. Patients who use nicotine and are unwilling to quit should be treated using the five A’s.
   c. Patients who use nicotine and are willing to quit should be treated using the five A’s.
   d. Patients who use nicotine and are willing to quit should be treated using the five R’s.

2. According to the AHRQ Clinical Practice Guideline, what is the minimum amount of time health care professionals should interact with patients to increase cessation rates?
   a. 5 minutes
   b. 10 minutes
   c. 25 minutes
   d. 90 minutes

3. According to Clinical Practice Guidelines, nicotine cessation is more effective when __________.
   a. medication and counseling are provided
   b. no medication and counseling are provided
   c. only counseling is provided
   d. only medication is provided

4. Which questionnaire is a standard instrument used to assess the intensity of physical addiction?
   a. Fagerström Test
   b. General Sociology Smoking Survey
   c. Ready to Quit Survey
   d. Why Do I Smoke? Quiz

5. How many times does the average smoker attempt to quit nicotine in his or her lifetime?
   a. 1 to 2 times
   b. 3 to 5 times
   c. 6 to 9 times
   d. 10 to 15 times

6. Which questionnaire can be used to determine the patient’s willingness to quit nicotine?
   a. Fagerström Test
   b. General Sociology Smoking Survey
   c. Ready to Quit Survey
   d. Why Do I Smoke? Quiz

7. Which of the following common signs of nicotine withdrawal should patients be educated about?
   a. Anxiety
   b. Decreased blood pressure and heart rate
   c. Increase in appetite and weight gain
   d. All the above

8. What is the difference between a slip and a relapse?
   a. A slip is a failure; a relapse is not a failure.
   b. A slip is a one-time mistake that is quickly corrected; a relapse is returning to using nicotine.
   c. A slip is not a failure, but the patient will never successfully quit; a relapse is a failure.
   d. A slip is returning to using nicotine; a relapse is a one-time mistake that is quickly corrected.

9. How should the pharmacist identify common triggers associated with nicotine use?
   a. Ask the patient’s family or friends.
   b. Modify the patient’s behavior.
   c. Review the comments in the patient’s nicotine log.
   d. Tell the patient to go to places where smoking isn’t allowed.

10. The last meeting with a patient should be ________.
    a. before he or she quits smoking
    b. used to address any concerns from the previous nicotine cessation sessions
    c. less than 5 minutes
    d. optional

Circle one (1) Answer:

1. a  b  c  d
2. a  b  c  d
3. a  b  c  d
4. a  b  c  d
5. a  b  c  d
6. a  b  c  d
7. a  b  c  d
8. a  b  c  d
9. a  b  c  d
10. a  b  c  d

CPE Home Study Evaluation

1. Rate this lesson: (Excellent) 5 4 3 2 1 (Poor)
2. Did this lesson meet each of its objectives? Yes No
3. Was the content without commercial bias? Yes No
   If not, please explain______________________________
4. Did the lesson meet your educational/practice needs? Yes No
5. Comments/future topics are welcome.______________________________

The deadline for this quiz is December 12, 2018.

Keep the TOP portion for your records. Return the BOTTOM portion to the NPA office. Or, take this quiz online at www.npharm.org
WE HOPE YOU WILL JOIN US!

Please join us at this year’s NPA Annual Convention, June 8 & 9, 2018, at The Marriott Cornhusker Hotel in Lincoln, Nebraska.

The convention is full of networking opportunities with pharmacy colleagues, as well as continuing education programs for pharmacists and pharmacy technicians designed to improve and expand practices for better patient care. New this year is a Friday breakfast program sponsored by Shire. We are also excited to have a very special guest - Nebraska Volleyball Head Coach, John Cook - speaking at lunch on Saturday.

The NPA strives to provide the best member experience and to help you meet the challenges of the many changes in healthcare. The convention is a prime time to exchange information, network, and stay on top of education. Your participation makes the convention stronger, our community stronger, and patient care stronger.
Friday, June 8
Schedule of Events

6:30 am – 4:30 pm
Registration

6:45 am – 7:45 am (Doors close at 7:00 am)
Breakfast sponsored by Shire
Von Vendi, a Treatment Made Specifically for Von Willebrand’s Disease
Mary Lynn Moody, BSPharm, Clinical Associate Professor and Assistant Dean for Business Development at the University of Illinois at Chicago

8:00 am - 9:00 am
Pharmacogenomic Services in the Pharmacy
Theresa Tolle, BPharm, FAPhA, Pharmacist/Owner, Bay Street Pharmacy
ACPE UAN 0128-0000-18-030-L04-P/T Knowledge-based CPE Activity
Program Objectives:
1. Define and list the basics of pharmacogenetics.
2. Describe how to incorporate pharmacogenetics into community pharmacy practice.
3. Identify a pharmacogenetic protocol and how to overcome barriers.

9:00 am – 9:15 am
Break

9:15 am – 10:15 am
What Pharmacists and Pharmacy Technicians Need to Know About Naloxone
Katharine Reisbig, PharmD, BCPS, Nebraska Medicine, Clinical Services Pharmacy Manager
ACPE UAN 0128-0000-18-029-L01-P/T Knowledge-based CPE Activity
Program Objectives:
1. Identify the signs and symptoms of overdose.
2. Describe how to administer naloxone.

10:15 am – 10:30 am
Break

10:30 am – 11:30 am
HIPAA: A Review
Abbie Widger, Attorney at Law, Johnson Flodman Guenzel & Widger Law Firm
ACPE UAN 0128-0000-18-028-L03-P/T Knowledge-based CPE Activity
Program Objectives:
1. Define HIPAA and review regulations.
2. Examine recent cases and settlements.
3. Describe HIPAA policies and procedures regarding electronic devices and all types of social media.
4. Devise a plan for the use of and challenges of using electronic devices in facilities.
5. Identify recent texting guidelines.

11:30 am – 1:00 pm
LUNCH WITH EXHIBITORS

1:00 pm – 2:00 pm
NETWORK CONNECTIONS
• Academia/Specialty Practice Network – Nicole White, Chair
• Chain Network – Linda Guzman- Gonzales, Chair
• Independent Network – Trevor Bertsch, Chair
• Hospital/Health-System Network – Jerome Wohleb, Chair
• Long-Term Care Network – Sheryl Havermann, Chair
• New Practitioner Network – Jacelyn Watt, Chair
• Pharmacy Technicians – Christina Gerard, CPhT

2:00 pm – 2:15 pm
Break

2:15 pm – 3:45 pm
Motivational Interviewing: Strategies to Improve Understanding Between Pharmacists, Pharmacy Technicians, and their Patients
Patty Hawk, PhD, Associate Professor/Department Chair of Communication Studies, Nebraska Wesleyan University
ACPE UAN 0128-0000-18-027-L04-P/T Application-based CPE Activity
Program Objectives:
1. Identify ways to engage patients authentically as a way to reach understanding.
2. Demonstrate effective communication with patients through dialogue.

3:45 pm – 4:00 pm
Break

4:00 pm – 5:00 pm
The Doctor Ordered, Huh? And You Wanna Do What?
Rusty McKune, ATC, Sports Medicine Coordinator, Nebraska Medicine
ACPE UAN 0128-0000-18-026-L04-P/T Knowledge-based CPE Activity
Program Objectives:
1. Describe how to treat and support orthopedic conditions.
2. Identify when to refer an athletic injury for treatment.
3. Review nutritional options for athletes.

5:00 pm – 7:00 pm
NPA MEMBERSHIP MEETING, NPA AWARDS & SOCIAL

Have a Question?  |  npharm.org/2018AnnualConvention  |  info@npharm.org  |  402-420-1500
### Saturday, June 9

#### Schedule of Events

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>6:30 am – 3:00 pm</td>
<td>Registration</td>
</tr>
<tr>
<td>6:45 am – 7:45 am (Doors close at 7:00 am)</td>
<td>Breakfast Program <em>(Topic &amp; Speaker TBA)</em></td>
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<tr>
<td>8:00 am - 9:30 am</td>
<td><strong>5 Keys to Improving Your Financial Fitness</strong></td>
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<td></td>
<td>Tim Church, PharmD, BCACP, CDE, Team Member, Your Financial Pharmacist</td>
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<td>ACPE UAN 0128-0000-18-025-L04-P/T Application-based CPE Activity</td>
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<tr>
<td></td>
<td>Program Objectives:</td>
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<tr>
<td></td>
<td>1. Explain why income does not equal financial success.</td>
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<td></td>
<td>2. Identify current financial health by calculating net worth.</td>
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<td></td>
<td>3. Review financial goals and create a budget that helps transform them into reality.</td>
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<td></td>
<td>4. Identify major ways to protect income and determine adequate insurance coverage.</td>
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<td>5. Analyze options to repay student loans and other debt and choose a plan that is consistent with goals.</td>
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<tr>
<td>9:30 am – 9:45 am</td>
<td>Break</td>
</tr>
<tr>
<td>9:45 am – 10:45 am</td>
<td><strong>Caring for Patients with Behavioral Health Disorders: Developing Competence and Confidence</strong></td>
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<td>Carla Cobb, PharmD, BCPP, Psychiatric Pharmacist, Capita Consulting</td>
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<td>ACPE UAN 0128-0000-18-024-L01-P/T Application-based CPE Activity</td>
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<tr>
<td></td>
<td>Program Objectives:</td>
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<tr>
<td></td>
<td>1. Describe factors that impact the care of patients with behavioral health (BH) disorders including access to care, stigma, and adherence.</td>
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<td></td>
<td>2. Identify common opportunities for pharmacists to improve the health outcomes of patients with BH disorders.</td>
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<td></td>
<td>3. Explain methods for improving medication adherence for patients with BH disorders.</td>
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<tr>
<td>10:45 am – 11:00 am</td>
<td>Break</td>
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<tr>
<td>11:00 am – Noon</td>
<td><strong>Drug Theft and Robbery</strong></td>
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<tr>
<td></td>
<td>Chad Robacker, Group Supervisor, Tactical Diversion Squad, DEA Omaha</td>
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<td></td>
<td>ACPE UAN 0128-0000-18-023-L04-P/T Knowledge-based CPE Activity</td>
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<td></td>
<td>Program Objectives:</td>
</tr>
<tr>
<td></td>
<td>1. Identify common mechanisms for employee theft of controlled substances.</td>
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<td></td>
<td>2. Describe measures to prevent a pharmacy robbery.</td>
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<td></td>
<td>3. Explain what to do during a robbery.</td>
</tr>
<tr>
<td></td>
<td>4. List the steps to be taken after a robbery or burglary.</td>
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<tr>
<td>Noon – 1:30 pm</td>
<td><strong>Lunch</strong></td>
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<tr>
<td>12:30 pm – 1:30 pm</td>
<td><strong>Dream Big, Dream Like A Champion</strong></td>
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<td>Nebraska Volleyball Coach, John Cook</td>
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<tr>
<td>1:30 pm – 3:00 pm</td>
<td><strong>Life Planning – Living a Life with Purpose</strong></td>
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<td>Dan Krick, Vice President, Organizational Development, Hexagon Lincoln</td>
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<td></td>
<td>ACPE UAN 0128-0000-18-022-L04-P/T Application-based CPE Activity</td>
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<td>Program Objectives:</td>
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<tr>
<td></td>
<td>1. Describe the benefits of a Life Plan.</td>
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<td>2. Examine the process of living a life that is consistent with one’s purpose.</td>
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<tr>
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<td>3. Prepare a Life Plan “template” that will help provide the framework for purpose, dreams, and goals regarding well-being components.</td>
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<tr>
<td>3:00 pm – 3:15 pm</td>
<td>Break</td>
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<tr>
<td>3:15 pm – 4:15 pm</td>
<td><strong>Pharmacy Law</strong></td>
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<td>Joni Cover, Chief Executive Officer, Nebraska Pharmacists Association; and Marcia Mueting, PharmD, Nebraska Pharmacists Association</td>
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<td></td>
<td>ACPE UAN 0128-0000-18-021-L03-P/T Application-based CPE Activity</td>
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<tr>
<td></td>
<td>Program Objectives:</td>
</tr>
<tr>
<td></td>
<td>1. Describe how recent revisions in statutes and regulations impact the practice of pharmacy.</td>
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<tr>
<td></td>
<td>2. Review Uniform Credentialing Act requirements.</td>
</tr>
</tbody>
</table>
Pharmacist & Technician Registration

Full Registration (Friday & Saturday)
Includes up to 11.50 hours of continuing pharmacy education for pharmacists and pharmacy technicians; access to handouts online; breakfasts; morning and afternoon refreshment breaks; lunch with exhibitors; and evening social.

Friday Only Registration
Includes up to 5.50 hours of continuing pharmacy education for pharmacists and pharmacy technicians; access to handouts online; breakfast program; morning and afternoon refreshment breaks; lunch with exhibitors; and evening social.

Saturday Only Registration
Includes up to 6.00 hours of continuing pharmacy education for pharmacists and pharmacy technicians; access to handouts online; breakfast program; morning and afternoon refreshment breaks; and lunch.

Student/Guest Registration

Full Registration (Friday & Saturday)
Includes access to all continuing pharmacy education sessions; access to handouts online; breakfasts; morning and afternoon refreshment breaks; lunch with exhibitors; and evening social.

Friday Only Registration
Includes access to Friday’s continuing pharmacy education sessions; access to handouts online; breakfast program; morning and afternoon refreshment breaks; lunch with exhibitors; and evening social.

Saturday Only Registration
Includes access to Saturday’s continuing education sessions; access to handouts online; breakfast program; morning and afternoon refreshment breaks; and lunch.

Location & Accommodations
The host hotel for the NPA’s 2018 Annual Convention is The Marriott Cornhusker Hotel at 333 South 13th Street in Lincoln, Nebraska. For reservations, call 402-474-7474 and ask for the Nebraska Pharmacists group rate. Room block expires May 24, 2018.

Breakfast
The breakfast programs on Friday and Saturday are free to all registered convention attendees and are the only breakfast option provided by the NPA. CPE is not available.

Ticketed Events

Event Registration Only
Registration for Lunch with Exhibitors, Friday’s evening social, and Saturday’s lunch may be purchased as stand alone items. They do not include access to any continuing education sessions, morning breakfasts, refreshment breaks, or program materials.

Handouts
Speaker presentations and materials for the convention will be posted on the NPA website at www.npharm.org and available from the NPA convention app. Materials may be viewed or printed before and after the convention.

Cancellation & Refund Policy
We understand that circumstances arise that require you to cancel or send a substitute. Canceled registrations must be in writing. Cancellations received on or before May 25, 2018, will receive a refund in the amount paid less a 25% administrative fee. No refunds will be made after June 1, 2018. Please notify the NPA of any changes prior to the event to help facilitate the check-in process.

Exhibitors *at time of printing
AbbVie
Allergan
Avella Specialty Pharmacy
Boehringer-Ingelheim
Creighton University School of Pharmacy & Health Professions
Dakota Drug
Eli Lilly Diabetes
Janssen Pharmaceuticals
McKesson
Nebraska Health Information Initiative
Nebraska MEDS Drug Disposal
Nebraska Total Care

Novo Nordisk
Pfizer
Pfizer Vaccines
Pharmacists Mutual
QS/1 Pharmacy Management Software
RxPlus Pharmacies
Shire
Southeast Community College
Veltec Associates
Walgreens
WellCare Health Plans of Nebraska
Winter Wolf Consulting

Convention Sponsor
Creighton University School of Pharmacy & Health Professions
Nebraska Pharmacists Corporation
National Association of Chain Drug Stores
Shire

Welcome Sponsor
Genoa Healthcare
Smart-Fill

Donations
Pharmacists Mutual
Rx Systems
Continuing Education

The 2018 NPA Annual Convention is sponsored by the Nebraska Council for Continuing Pharmacy Education (NCCPE). NCCPE is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education. On Friday, June 8 and Saturday, June 9, 2018, pharmacists and pharmacy technicians may earn up to 11.5 contact hours (1.15 CEUs) of continuing pharmacy education (CPE) credits for attendance of the entire CPE activity and the completion of an activity evaluation. In order to receive CPE credits, participants must provide their NABP e-Profile ID number and birth date (MMDD). Credits will be reflected in the NABP CPE Monitor System no later than 45 days after the convention. For questions about CPE credits, call NCCPE at (402) 420-1500.

Target Audience

Programming has been designed for pharmacists, pharmacy technicians, and student pharmacists in all practice settings who take part in the overall healthcare of patients and Nebraska residents.

Exhibits

On Friday, June 8, exhibitors including pharmacy manufacturers, insurers, schools of pharmacy, and vendors will be on hand to discuss their newest products and services that may be a benefit to you.

Networking and Events

Connect with colleagues during breaks, meals, and the pharmacy social. During Saturday’s lunch, Husker Volleyball Coach, John Cook, will speak about his book, *Dream Like a Champion*, sharing the coaching and leadership philosophy that has enabled him to become one of the game’s winningest coaches. Coach will be available to sign copies of his book which is available for sale at amazon.com.
CONVENTION REGISTRATION

Please print

Name ___________________________________________ Phone ____________________________

Badge Name _____________________________________ Email __________________________________

Mailing Address __________________________________________________________

City/Zip ____________________________________________________________

Guest/Spouse Name (if applicable) __________________________________________

Convention Text Messages:

Cell Phone #_____________________________

Sign-up to receive text alerts regarding convention activities. Message and data rates may apply. Reply STOP to end or HELP for help.

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Early Bird On or Before 2018-05-16</th>
<th>On or After 2018-05-17</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full Registration (Friday &amp; Saturday)</strong></td>
<td>$230</td>
<td>$270</td>
<td>$_______</td>
</tr>
<tr>
<td>Pharmacist</td>
<td>$230</td>
<td>$270</td>
<td>$_______</td>
</tr>
<tr>
<td>NonMember Pharmacist</td>
<td>$330</td>
<td>$370</td>
<td>$_______</td>
</tr>
<tr>
<td>Technician/Student</td>
<td>$130</td>
<td>$170</td>
<td>$_______</td>
</tr>
<tr>
<td>NonMember Technician/Student</td>
<td>$180</td>
<td>$220</td>
<td>$_______</td>
</tr>
</tbody>
</table>

| **Friday Only Registration** | $160 | $200 | $_______ |
| Pharmacist                   | $160 | $200 | $_______ |
| NonMember Pharmacist         | $260 | $300 | $_______ |
| Technician/Student           | $100 | $140 | $_______ |
| NonMember Technician/Student | $150 | $190 | $_______ |

| **Saturday Only Registration** | $140 | $180 | $_______ |
| Pharmacist                   | $140 | $180 | $_______ |
| NonMember Pharmacist         | $240 | $280 | $_______ |
| Technician/Student           | $100 | $140 | $_______ |
| NonMember Technician/Student | $150 | $190 | $_______ |

| **Event Registration Only**  | $55  | $65  | $_______ |
| Friday Lunch & Exhibits      | $55  | $65  | $_______ |
| Friday Evening Social        | $45  | $55  | $_______ |
| Saturday Lunch               | $45  | $55  | $_______ |

| **Donations**                |       |       |       |
| NebPharmPAC                  | $_______ |       |       |
| Nebraska Pharmacy Foundation | $_______ |       |       |

**REGISTRATION TOTAL** $_______

Payment

- **Check** (Payable to the NPA)
  - Check # ____________________________

- **Credit Card**
  - # ____________________________
  - Exp. Date _____/______ Sec. Code ______
  - Signature ____________________________

Have a Question? | npharm.org/2018AnnualConvention | info@npharm.org | 402-420-1500

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Lincoln, NE 68516

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