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We Hear That

Pharmacist, John Krick, Lincoln, passed away December 31, 2016. Following graduation from the University of Nebraska College of Pharmacy, John worked at Family Drug and St. Elizabeth Hospital in Lincoln. He then owned and operated Meadow Lane Pharmacy, Lincoln, from 1978-2006, and worked the rest of his career at Walgreens. Our condolences to the Krick family!

NPA Lifetime Member, Robert Svanda, Ravenna, passed away January 4, 2017. Bob graduated from the University of Nebraska-Lincoln in 1953, and served in the U.S. Army Peacetime from 1954-1957, after which he returned home to join his father at Svanda Pharmacy, where Bob later became owner of the store. Our condolences to the Svanda family!

NPA Member, Ransom Varney, Broken Bow, passed away January 8, 2017. Ran graduated from the University of Nebraska-Lincoln and started working at Varney Rexall Drug. In 1978, Ran purchased the store from his father. In 1988 Varney Rexall became Varney Healthmart. In 2005, Ran sold his store to Marge Trytball, but continued to work relief for Barmore Drug in Lexington, Right Drug in Callaway, and Holcomb Pharmacy in Broken Bow. Our condolences to the Varney family!

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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.

Verification of Licensure or Registration
All pharmacy technicians in Nebraska were required to renew their registration on January 1, 2017. Pharmacists will renew their license in January 1, 2018.

Be sure to verify that ALL pharmacy staff have a current license or registration by checking the Nebraska Department of Health & Human Services (DHHS) License Information System (https://www.nebraska.gov/LISSearch/search.cgi). Pharmacy technicians registered on January 1, 2016 must also be certified by January 1, 2017.

DEA Registration Renewal Changes
Through a notice on its website (https://www.deadiversion.usdoj.gov/drugreg/index.html), the Drug Enforcement Administration (DEA) recently announced significant changes to its registration renewal process.

Effective January 1, 2017, the DEA is eliminating the informal grace period which the agency has previously allowed for registrants to renew their registrations. ONLY ONE renewal notice will be sent to each registrant’s “mail to” address approximately 65 days prior to the expiration date; no other reminders to renew the DEA registration will be provided.

The notice also advises that online capability to renew a DEA registration after the expiration date will no longer be available, and that failure to file a renewal application by midnight EST of the expiration date will result in the “retirement” of the registrant’s DEA number. The original DEA registration will not be reinstated. In addition, paper renewal applications will not be accepted the day after the expiration date. If DEA has not received the paper renewal application by the day of the expiration date, mailed in renewal applications will be returned and the registrant will have to apply for a new DEA registration.

Nebraska PDMP Information
The requirement to report all dispensed controlled substances for Nebraska pharmacies and pharmacies that mail medications to Nebraska addresses to the Nebraska Prescription Drug Monitoring Program (PDMP) operated by NeHII began on January 1, 2017. Pharmacists may access the PDMP at no cost and are encouraged to utilize the PDMP on a voluntary basis.

The PDMP website (http://dhhs.ne.gov/publichealth/PDMP/Pages/Home.aspx) has training materials and other general information for pharmacists, prescribers, and others. Questions about the PDMP can be sent to PDMP@NeHII.org

When Should OTCs be Tax-Exempt?
Simply having a prescription for an item does NOT make it tax-exempt. Nebraska regulation Title 316 Chapter 1-050.02B (Medicines and Medical Equipment) states, "Over-the-counter drugs that can be purchased without a prescription are taxable even when they are prescribed by a doctor." An item is tax-exempt if it is:

- insulin.
- for a Medicaid patient, billed to Medicaid.
- DME or medical supplies, dispensed pursuant to a prescription. (Examples include: insulin syringes; diabetic testing strips and associated supplies; crutches; and ostomy bags and associated supplies.)
- OTC medications such as Tylenol®, Pepcid AC®, or cough syrups are taxable, even if the patient has a prescription, unless the patient is covered by Nebraska Medicaid.

New Board Members
The NPA welcomes two new Board of Directors: Ken Kester and Kelly Hamilton.

Representing District 1: Ken Kester, PharmD, Catholic Health Services, Lincoln.
Ken says it a great privilege to serve on the NPA Board of Directors. He has spent most of his 31-year career as a pharmacist in hospital practice. He also has retail pharmacy experience, primarily as a moonlighter, but with a year of full-time work as well. He has served as the pharmacist member of the Nebraska Board of Health for six years, and has been a member of NPA’s Legislative Committee for many years. He looks forward to working on the Board to focus on the interest of pharmacists in Nebraska and the patients they serve.

Representing District 3: Kelly Hamilton, PharmD, U-Save Pharmacy, Holdrege.
Kelly believes that the NPA plays a vital role in advocating for and educating its members. In navigating all of changes and challenges in healthcare, is very important that practicing pharmacists are involved in discussions and decisions that affect the future of the profession and the care of. Kelly is honored to represent District 3 on the NPA Board of Directors.
New Drugs: Zinbryta, Ocaliva, and Epclusa

This CPE lesson was written by Christopher Zaleski, PharmD Candidate, University of Nebraska Medical Center College of Pharmacy, who does not have any conflicts of interest, nor does he have financial relationships with a commercial interest related to this activity.

Objectives
At the conclusion of this lesson, pharmacists and pharmacy technicians should be able to:
1. Identify the indication, therapeutic class, and pharmacologic action for each new drug.
2. Describe significant adverse effects, drug interactions, warnings, cautions, and important patient counseling information for each new drug.

Zinbryta™ (daclizumab)
Introduction
Multiple sclerosis (MS) is a disease characterized by an immune-mediated process in which the immune system attacks the protective coating around the nerves within the central nervous system (CNS). The body’s immune system dispatches T-cells that attack myelin within the CNS causing the formation of scar tissue. The damaged myelin sheath around the nerves alters nerve impulses traveling to and from the CNS. The misinterpretation or disruption in the transmission of nerve impulses within the CNS causes an array of adverse effects for patients.1

While the exact mechanism that causes MS remains unknown, researchers have recognized the importance of genetics involving the CD25 subunit of the interleukin-2 receptor (IL-2) found on T-cells. Researchers believe that patients with an increased expression of CD25 are at a higher risk for developing MS.2,3 In May 2016, based on the outcomes of two clinical trials (SELECT and DECIDE), the Food and Drug Administration (FDA) approved Biogen’s Zinbryta (daclizumab).

Daclizumab is a once monthly, self-administered subcutaneous injection that targets the CD25 subunit of IL-2 receptors.3,4,5

Indications
Daclizumab is an IL-2 receptor blocking monoclonal antibody used to treat adults suffering from relapsing forms of MS. The use of daclizumab is reserved for patients who have tried two or more MS therapies and continue to experience complications of the disease.6

Mechanism of Action
Daclizumab targets the CD25 subunit on high-affinity IL-2 receptors. By binding to the CD25 subunit, signaling at the high-affinity IL-2 receptor is antagonized. This increases signaling on those cells expressing an intermediate-affinity IL-2 receptor. The antagonism of CD25 and the increased signaling of intermediate-affinity IL-2 receptors is thought to confer a therapeutic benefit in patients suffering from MS by inducing the expression of natural killer cells that target T-cells and through the inhibition of T-cell activation.3

Dosage
Daclizumab is a once monthly, self-administered subcutaneous injection. It is available as a 150 mg/mL prefilled syringe. Each prefilled syringe is intended to be used as a single dose.6

Contraindications and Warnings
Daclizumab may cause severe and potentially life-threatening hepatic injury. It is contraindicated in patients with pre-existing hepatic disease or hepatic impairment characterized by alanine aminotransferase (ALT) and aspartate aminotransferase levels more than twice the upper limit of normal, as well as elevations in total bilirubin. Daclizumab is also contraindicated in patients with a history of autoimmune hepatitis or any other autoimmune condition involving the liver, and in patients with a history of hypersensitivity or anaphylaxis to any of the components found within the drug formulation.

Daclizumab carries two boxed warnings: one for hepatic injury as previously mentioned and another for other immune-mediated disorders. Other immune-mediated disorders include skin reactions, lymphadenopathy, and non-infectious colitis.

Because of the risk of hepatic injury and other immune-mediated disorders, prescribers, pharmacists, and patients must comply with a Zinbryta Risk Evaluation and Mitigation Strategy Program (www.zinbryta.rems.com or 1-800-456-2255).6

Adverse Effects
The most common adverse effects associated with daclizumab use include nasopharyngitis, upper respiratory tract infection, rash, influenza, dermatitis, oropharyngeal pain, bronchitis, eczema, lymphadenopathy, tonsillitis, and acne. Other common adverse effects noted in the SELECT clinical trials include pharyngitis and rash. When compared with Avonex (interferon beta-1a), daclizumab exhibited a > 2% higher incidence of the above adverse effects. In addition, depression, pharyngitis rhinitis, anemia, pyrexia, and increased
Significant Drug Interactions
Concomitant use of additional hepatotoxic agents with daclizumab should be used with extreme caution. If dual hepatotoxic therapy is warranted, the patient should be monitored by a healthcare professional for signs and symptoms of decreasing liver function. These signs and symptoms include nausea or vomiting, stomach pain, unusual tiredness, not wanting to eat, yellowing of the skin or whites of the eyes, and dark urine.9

Patient Counseling
Daclizumab should be kept in the original container to protect from light. It should be stored in a refrigerator between 36°F and 46°F. Do not freeze or use if frozen. Do not store the drug above a temperature of 86°F. Daclizumab can be stored at room temperature for up to 30 days. If the drug has reached room temperature, do not place it back in the refrigerator. Dispose of daclizumab if it has not been at room temperature or out of the refrigerator for more than 30 days.

Patients should be instructed to remove daclizumab from the refrigerator 30 minutes prior to injection to allow the drug to reach room temperature. Inspect daclizumab before administration. The drug is a colorless to slightly yellow, clear to slightly opaque solution. Do not use daclizumab if it is cloudy or discolored.

Patients should be trained on proper use for self-administration of the subcutaneous injection. Injection sites include the thigh, abdomen, and back of the upper arm.

Potential adverse effects should be discussed with patients. Counsel patients to contact their healthcare provider if they experience signs and symptoms of liver function, skin reactions such as rash or skin irritation, tender, painful, or swollen lymph nodes, any new and unexplained symptoms affecting any part of the body, or intestinal problems such as colitis. Symptoms of colitis include fever, stomach pain, blood in the stool, or diarrhea that does not go away.6

Ocaliva™ (obeticholic acid)

Introduction
Primary biliary cholangitis (PBC) is an autoimmune, chronic liver condition characterized by the destruction or absence of hepatic bile ducts, granulomatous cholangitis, and fibrosis of the hepatic portal vein that, over time, may progress to hepatic biliary cirrhosis. While the exact etiology of PBC remains unknown, researchers are continuing to explore different treatment avenues for patients suffering from PBC. Of particular importance is Intercept Pharmaceuticals’ Ocaliva (obeticholic acid) which was approved by the FDA in May 2016. Obeticholic acid targets a specific receptor in the bile acid synthesis pathway known as the Farnesoid X receptor (FXR).8

Indications
Ocaliva (obeticholic acid) is indicated for the treatment of PBC. It may be used as combination therapy with ursodiol in patients with an inadequate response to ursodiol alone or as monotherapy in those patients unable to tolerate ursodiol.9

Mechanism of Action
Obeticholic acid is an agonist at Farnesoid X receptors. It is different than ursodiol in that ursodiol has no activity at FXRs. FXRs are nuclear receptors that play an important role in bilirubin metabolism within the liver, intestines, and kidneys. Furthermore, FXRs play additional roles in bile acid synthesis via the regulation of gene expression of cholesterol 7 alpha-hydroxylase, carbohydrate and lipid metabolism, regulation of insulin sensitivity, and protection fatty liver conditions.5,10 Obeticholic acid exhibits its actions on FXR receptors due to a small, yet significant, chemical modification involving an ethyl substitution on the sixth carbon within the molecular skeleton of the drug.10

Figure 1 describes this change.

Dosage
See Table 1 for dosing.

Contraindications and Warnings
Obeticholic acid is contraindicated in those patients with a complete biliary obstruction. Patients who are taking obeticholic acid should be warned of the signs and symptoms of worsening hepatic impairment including jaundice, worsening ascites, and primary biliary flare. Moreover, obeticholic acid carries the potential for reducing HDL cholesterol. Additionally, patients taking obeticholic acid are at an increased risk of experiencing severe pruritus characterized by intense itching interfering with activities of daily living.9,10

Adverse Effects
In addition to pruritis, reductions in HDL-C, and liver-related adverse events as previously discussed, the most common adverse effects associated with obeticholic acid use are abdominal pain, fatigue, rash, arthralgia, oropharyngeal pain, dizziness, constipation, peripheral edema, palpitations, pyrexia, thyroid function abnormality, and eczema.9,10,11
**Table 1. Obeticholic acid dosing**

<table>
<thead>
<tr>
<th>Dosing to be initiated in adult patients who have not achieved an adequate biochemical response to an appropriate dosage of ursodiol for at least 1 year or are intolerant to ursodiol.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Starting Dose</strong></td>
</tr>
<tr>
<td><strong>Dose Titration</strong></td>
</tr>
<tr>
<td><strong>Maximum Dose</strong></td>
</tr>
<tr>
<td><strong>Management of patients with intolerable pruritus associated with obeticholic acid use.</strong></td>
</tr>
<tr>
<td>Patients intolerant to 5 mg once daily*</td>
</tr>
<tr>
<td>Patients intolerant to 10 mg once daily*</td>
</tr>
<tr>
<td>Hepatic impairment dosage adjustment (Child-Pugh Class B and C).</td>
</tr>
<tr>
<td><strong>Starting Dose</strong></td>
</tr>
<tr>
<td><strong>Dose Titration</strong></td>
</tr>
</tbody>
</table>

*Patients may also add an antihistamine or bile acid resin or therapy with obeticholic acid may be temporarily interrupted for up to 2 weeks followed by restarting at a reduced rate.

**Significant Drug Interactions**

Taking obeticholic acid with bile acid resins like cholestyramine, colestipol, or colesevelam may reduce the absorption, systemic exposure, and efficacy of obeticholic acid. Patients should be advised to take obeticholic acid at least four hours before or after taking a bile acid resin. In clinical trials, it was noted that patients taking warfarin with obeticholic acid saw a decrease in International Normalized Ratio (INR). These patients should have their INR monitored closely and their warfarin dosage by a healthcare professional adjusted as necessary. Additionally, obeticholic acid may increase exposure of medications that are substrates for CYP1A2 (e.g. theophylline, tizanidine). Patients should monitor for increased adverse effects associated with concomitant use.

**Patient Counseling**

Obeticholic acid may be taken without regard to food. Patients should be advised to take obeticholic acid at least four hours before or after taking a bile acid binding resin. Furthermore, patients should be advised to report any symptoms of worsening liver function including increased fatigue, yellowing of the skin or whites of the eyes, abdominal pain, nausea and vomiting, or bleeding that does not stop after a few minutes. Patients should consult their healthcare professional if they begin to experience pruritus or an increase in the severity of pruritus. Patients should also be advised to undergo laboratory tests to detect any changes in lipid levels.

**Epclusa® (sofosbuvir/velpatasvir)**

**Introduction**

Hepatitis C virus (HCV) is a common blood-borne virus that replicates within hepatocytes in the liver. It is a single-stranded RNA virus of the family Flaviviridae. HCV is categorized into six different genotypes ranging from genotype 1 to genotype 6. In an HCV infection, hepatocytes are activated for apoptosis. The programmed death of hepatocytes may lead to cirrhosis of the liver, end-stage liver disease, or hepatocellular carcinoma.

Even with advances in medication therapy, HCV remains a treatment challenge. Generally, genotypes 1, 2, and 3 respond well to therapy, while genotypes 4, 5, and 6 are more difficult to treat. Current therapies for HCV infection are mainly targeted at specific HCV genotypes.

**Mechanism of Action**

Sofosbuvir is a prodrug that works by blocking the roles of NS5A. It is a single-stranded, RNA virus that replicates within liver cells. NS5B is a non-structural protein that possesses an important role in viral RNA replication. It is a polymerase that demonstrates a vital role in viral RNA synthesis. Velpatasvir is an antiviral agent used as an inhibitor of NS5A, another non-structural protein that possesses an important role in cell growth and proliferation associated with HCV. Velpatasvir exerts its therapeutic benefit by blocking the roles of NS5A. The inhibition of NS5A prevents the replication of viral HCV RNA.

**Dosage**

Sofosbuvir/velpatasvir is a fixed dose oral tablet containing 400 mg of sofosbuvir and 100 mg of velpatasvir. Patients without cirrhosis of the liver and patients with mild (Child-Pugh Score A) compensated cirrhosis should take one sofosbuvir/velpatasvir tablet by mouth once daily for twelve weeks. Patients with moderate to severe (Child-Pugh Scores B to C) decompensated cirrhosis should take one sofosbuvir/velpatasvir tablet by mouth once daily concomitantly with a daily ribavirin regimen for twelve weeks. Ribavirin should be dosed by weight and given with food.

June 2016, the FDA approved Gilead’s Epclusa (sofosbuvir/velpatasvir) for the treatment of HCV across all six genotypes. Phase III clinical trials demonstrated an overwhelming success rate in patients taking the combination product with 95-99% of patients with no virus upon detection after twelve weeks of therapy. Currently, the medication is only available through specialty pharmacies.
It should be given as 1000 mg per day for patients weighing less than 75 kg and 1200 mg per day for patients weighing at least 75 kg, divided in two daily doses.\textsuperscript{17}

**Contraindications and Warnings**

Sofosbuvir/velpatasvir in combination with ribavirin is contraindicated in patients for whom ribavirin is contraindicated. Post-market studies have demonstrated a safety concern with the concomitant use of sofosbuvir/velpatasvir and amiodarone. Patients are warned of serious symptomatic bradycardia potentially leading to fatal cardiac adverse events. If patients need to begin amiodarone therapy, they should undergo cardiac monitoring via in-patient telemetry for the first 48 hours, then outpatient or self-monitoring of heart rate should be done on a daily basis for at least the first 2 weeks of treatment. Due to the extended half-life of amiodarone, these same monitoring parameters should be in place if a patient is discontinuing amiodarone therapy.\textsuperscript{17}

**Adverse Effects**

In the ASTRAL-1, ASTRAL-2, and ASTRAL-3 clinical trials evaluating sofosbuvir/velpatasvir therapy varying across the different HCV genotypes in patients with (Child-Pugh Score A) or without compensated cirrhosis, adverse events observed were headache, fatigue, nasopharyngitis, nausea, insomnia, diarrhea, asthenia, arthralgia, cough, back pain, and myalgia. All of the mentioned adverse events were seen in at least 5% of the patient population within the study.\textsuperscript{14,15}

The ASTRAL-4 trial evaluated therapy with sofosbuvir/velpatasvir compared to sofosbuvir/velpatasvir with ribavirin in patients with moderate to severe (Child-Pugh Score B or C) decompensated cirrhosis. Additional adverse effects that were noted included pruritus, muscle spasm, dyspnea, and anemia. There were also increased hematologic events in the ribavirin arm characterized by reduced hemoglobin level, reduced lymphocyte count, and reduced neutrophil count.\textsuperscript{16}

Overall, the most common adverse effects noted with sofosbuvir/velpatasvir use were headache and fatigue. The most common adverse effect noted with

### Table 2.
**Drug interactions with sofosbuvir/velpatasvir**\textsuperscript{17}

<table>
<thead>
<tr>
<th>Drug/Class</th>
<th>Outcome</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antacids</td>
<td>Decreased [velpatasvir]</td>
<td>Separate dosing by at least 4 hours</td>
</tr>
<tr>
<td>H2 antagonists</td>
<td>Decreased [velpatasvir]</td>
<td>May be given with or 12 hours apart from sofosbuvir/velpatasvir in a dose that does not exceed the equivalent of famotidine 40 mg twice daily</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>Decreased [velpatasvir]</td>
<td>Not recommended. Administer sofosbuvir/velpatasvir with food 4 hours before omeprazole 20 mg</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Serious symptomatic bradycardia</td>
<td>Avoid combination. If the combination is medically necessary, cardiac monitoring via in-patient telemetry for the first 48 hours, then outpatient or self-monitoring of heart rate should be done on a daily basis for at least the first 2 weeks of treatment should be initiated</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Increased [digoxin]</td>
<td>Monitor digoxin levels. Refer to digoxin prescribing information for dosage recommendations</td>
</tr>
<tr>
<td>Topotecan</td>
<td>Increased [topotecan]</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Anticonvulsants (carbamazepine, phenytoin, phenobarbital, oxcarbazepine)</td>
<td>Decreased [sofosbuvir/velpatasvir]</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Antimycobacterials (rifabutin, rifampin, rifapentine)</td>
<td>Decreased [sofosbuvir/velpatasvir]</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Decreased [velpatasvir]</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Tipranavir/ritonavir</td>
<td>Decreased [sofosbuvir/velpatasvir]</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Increased [tenofovir]</td>
<td>Monitor for tenofovir-associated adverse effects. Refer to tenofovir prescribing information for dosing recommendations and renal monitoring</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Increased [rosuvastatin]</td>
<td>Max of 10 mg of rosuvastatin per day</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Increased [atorvastatin]</td>
<td>Monitor for statin side effects</td>
</tr>
<tr>
<td>St. John’s Wort</td>
<td>Decreased [sofosbuvir/velpatasvir]</td>
<td>Avoid use</td>
</tr>
</tbody>
</table>
sofosbuvir/velpatasvir and ribavirin in patients with decompensated cirrhosis include fatigue, anemia, nausea, headache, insomnia, and diarrhea. Incidence of these adverse effects associated with sofosbuvir/velpatasvir use, with or without ribavirin, was > 10%.17

**Significant Drug Interactions**

Patients taking amiodarone in combination with sofosbuvir/velpatasvir are at an increased risk of experiencing serious symptomatic bradycardia that may potentiate fatal cardiac adverse events. The combination of the two regimens is not recommended. Patients taking beta blockers or digoxin may also be at risk. Acid-reducing agents including antacids, H2 antagonists, and proton pump inhibitors may decrease systemic velpatasvir concentration. Sofosbuvir/velpatasvir may increase the concentration of topotecan and anticonvulsant agent. Anticonvulsant agents including carbamazepine, phenytoin, phenobarbitol, and oxcarbazepine, as well as antinocycobacterials including rifabutin, rifampin, and rifapentin may decrease systemic concentrations of both sofosbuvir and velpatasvir. Certain HIV antiretroviral agents including efavirenz may decrease velpatasvir concentrations and the combination of tipranavir and ritonavir may decrease systemic exposure of both sofosbuvir and velpatasvir. Additionally, patients receiving regimens containing tenofovir may see increased tenofovir levels. Sofosbuvir/velpatasvir may also increase concentrations of certain HMG-CoA reductase inhibitors including rosuvastatin and atorvastatin. It is not recommended that patients take St. John’s Wort, as this has demonstrated decreased concentrations of both sofosbuvir and velpatasvir. Refer to Table 2 for drug interactions.

**Patient Counseling**

Patients taking amiodarone or beta blockers, or patients with a pacemaker should be advised about the signs of bradycardia including syncope, dizziness, weakness, fatigue, or chest pain. Patients should immediately consult their healthcare professional if any of these symptoms present. Patients should avoid pregnancy during combination treatment of sofosbuvir/velpatasvir and ribavirin and continue for six months after completion of treatment. Patients should be advised that antacids should be separated by four hours from sofosbuvir/velpatasvir dosing. H2 antagonists may be given with or without two hours apart from sofosbuvir/velpatasvir in a dose that does not exceed famotidine 40 mg twice daily. Patients taking proton pump inhibitors should take sofosbuvir/velpatasvir four hours prior to omeprazole 20 mg tablets or capsules. Sofosbuvir/velpatasvir may be taken without regard to food. Patients should notify their prescriber of all medications they are taking including OTC and herbal/natural products.17
New Drugs: Zinbryta, Ocaliva, and Epclusa

Quiz #1, February 2017, ACPE #0128-0000-17-015-H01-P/T

1. How often is daclizumab administered?
   a. Once daily
   b. Once weekly
   c. Once monthly
   d. Once every 6 months

2. Daclizumab targets:
   a. The CD4 subunit on MHC Class II receptors
   b. The CD11c subunit of fibrinogen
   c. The CD16 subunit on IgG antibodies
   d. The CD25 subunit on high-affinity IL-2 receptors

3. Daclizumab carries two boxed warnings. One is for immune-mediated disorders, the other is for:
   a. Cerebrovascular events
   b. Hepatic injury
   c. Nephrotoxicity
   d. Thrombocytopenia

4. How long may a patient store daclizumab at room temperature before it must be discarded?
   a. 30 days
   b. 35 days
   c. 40 days
   d. 45 days

5. Obeticholic acid is indicated to treat which condition?
   a. Cerebrovascular events
   b. Hepatitis C virus
   c. Multiple Sclerosis
   d. Primary biliary cholangitis

6. Obeticholic acid targets which receptors within the liver?
   a. Farnesoid X receptors
   b. Glucocorticoid receptors
   c. Liver X receptors
   d. Peroxisome proliferator-activated receptor gamma

7. What is the starting dose of obeticholic acid in a patient who has not achieved an adequate response to ursodiol therapy for at least one year and does not suffer from Child-Pugh class B or C hepatic impairment?
   a. 5 mg by mouth one time daily
   b. 10 mg by mouth one time daily
   c. 5 mg by mouth one time weekly
   d. 10 mg by mouth one time weekly

8. Sofosbuvir/velpatasvir is indicated to treat which genotype(s) of HCV?
   a. 1, 2, and 3 only
   b. 4, 5, and 6 only
   c. 1 only
   d. All 6 genotypes

9. What is the maximum dose of rosuvastatin a patient may take per day while taking sofosbuvir/velpatasvir?
   a. 5 mg
   b. 10 mg
   c. 20 mg
   d. 40 mg

10. Patients are at an increased risk of serious symptomatic bradycardia if taking sofosbuvir/velpatasvir with which other drug?
    a. Amiodarone
    b. Atorvastatin
    c. Carbamazepine
    d. Lisinopril

---

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 Nebraska Mortar & Pestle
Distinguished Scientist Rongshi Li, Ph.D.

Dr. Rongshi Li, Professor, Department of Pharmaceutical Sciences, has been named one of ten Distinguished Scientists on the UNMC campus. 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.

Dr. Li's research focus is antibiotic and anti-cancer drug discovery. The goal of his research is to discover novel antibiotic and anticancer therapeutics. He has been using innovative approaches including but not limited to fragment-based, structure-guided and natural product-derived design and synthesis of small molecules to develop antibiotic and anticancer agents.

His research will make a difference because these novel antibiotic and anticancer agents target drug resistance. Our novel natural product derivatives exhibit unique activities against both Gram-positive and Gram-negative bacteria, and anticancer properties with high potency and selectivity. They display a desirable pharmacokinetic profile, good bioavailability and no toxicities.

Dr. Li, along with the other award recipients, will be recognized at a ceremony in January. Congratulations to Dr. Li.

New Faculty

We would like to welcome Daren Knoell, Pharm.D., the new chair in the Department of Pharmacy Practice, to the College of Pharmacy. He joined the faculty in October.

Dr. Knoell received his Pharm.D. from UNMC College of Pharmacy. He comes to us from the Ohio State University. His wife, Karen, also a graduate of UNMC College of Pharmacy, has joined Nebraska Medicine as the Pharmacy Case Management Coordinator.

Dr. Knoell’s focus of study is to better understand the pathogenesis of lung disease that, in turn, will reveal new biological insight to prevent or mitigate disease. His laboratory was the first to discover that zinc and its metabolism, through a family of proteins known as zinc transporters, is critical in preventing lung injury and maintaining host defense against infection. Most recently, this line of investigation has focused on zinc metabolism in cell, animal and human studies that have revealed novel insight into zinc coordination over innate immune function through molecular control of an integral signaling pathways that impact lung function.

New Investigators

Martin Conda-Sheridan, Ph.D., Assistant Professor, department of Pharmaceutical Sciences, and Kim Scarsi, Pharm.D., Associate Professor, department of Pharmacy Practice, have been named New Investigators on the UNMC campus. 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. Conda-Sheridan’s research focus is Nanotherapeutics.

The goal of his research is to merge material sciences and medicinal chemistry. He wants to develop nanostructures and small molecules that can treat bacterial infections and cancer.

Dr. Scarsi’s research focus is HIV pharmacotherapy.

The goal of her research is to optimize medication therapy for patients living with HIV. The focus of her research is influenced by her work in low- and middle-income countries, where there are unique issues affecting women living with HIV, as well as men and women who are co-infected with HIV and tuberculosis (TB).

Her research will make a difference in the lives of patients living with HIV and TB by providing evidence that can be used to optimize medication therapy for people throughout the world.

Congratulations to Drs. Conda-Sheridan and Scarsi.
LEGISLATIVE BILL SUMMARY
One Hundred Fifth Legislature, First Session
current as of February 10, 2017

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<tr>
<th>Bill Number</th>
<th>Sponsor</th>
<th>Committee</th>
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<th>NPA Position</th>
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<tr>
<td>LB 18</td>
<td>Senator Kolterman</td>
<td>Health &amp; Human Services Committee</td>
<td>1/18/2017</td>
<td>Dental Assistants/Dental Hygienists Licensure Would establish requirements for expanded function dental assistants and expanded function dental hygienists. Would authorize licensed dental hygienists, upon completion of education and testing approved by the Board, to write prescriptions for mouth rinses and fluoride products that help decrease risk for tooth decay.</td>
<td>Watch</td>
<td>General File</td>
</tr>
<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 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 Would require a Remote Sellers (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.</td>
<td>Support</td>
<td>In Committee</td>
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<tr>
<td>LB 64</td>
<td>Senator Hansen</td>
<td>Health &amp; Human Services Committee</td>
<td>1/19/2017</td>
<td>Adrenal Insufficiency Diagnosis Information and Support Act Would require healthcare practitioners to deliver an information support sheet posted by the Division of Public Health of the Department of Health and Human Services on its website to patients diagnosed with adrenal insufficiency.</td>
<td>Watch</td>
<td>In Committee</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 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 88</td>
<td>Senator Blood</td>
<td>Health &amp; Human Services Committee</td>
<td>2/15/2017</td>
<td>Temporary Credentials for Military Spouses Would authorize the Department, upon the recommendation of the appropriate board to issue a temporary credential to a military spouse complying with specified requirements pending issuance of the applicable credential under the Uniform Credentialing Act.</td>
<td>Support</td>
<td>In Committee</td>
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### Legislative Bill Summary

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<th>Bill</th>
<th>Senator</th>
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<th>Bill Title</th>
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<tr>
<td>LB 92</td>
<td>Kolterman</td>
<td>Banking, Commerce &amp; Insurance Committee</td>
<td>2/13/2017</td>
<td><strong>Telehealth</strong> Would require certain health carriers to provide coverage for services delivered through telehealth. Would prohibit health carriers, including self-funded employee benefits plans not otherwise exempted by federal law, from excluding in any policy a service from coverage solely because the service is delivered through telehealth and is not provided through in-person consultation or contact between a licensed healthcare provider and a patient.</td>
<td>Support</td>
<td>In Committee</td>
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<td>LB 117</td>
<td>Hilkemann</td>
<td>Health &amp; Human Services Committee</td>
<td>1/27/2017</td>
<td><strong>Investigational Drug Use Act</strong> 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.</td>
<td>Watch</td>
<td>In Committee</td>
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<tr>
<td>LB 165</td>
<td>Brewer</td>
<td>Judiciary Committee</td>
<td>2/22/2017</td>
<td><strong>Federal Immigration Verification System</strong> 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</td>
<td>Position</td>
<td>Status</td>
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<td><strong>LB 166</strong>&lt;br&gt;Senator Kolterman&lt;br&gt;Health &amp; Human Services Committee&lt;br&gt;Hearing 1/27/2017</td>
<td>Pharmacy Practice Act - Uniform Controlled Substances Act&lt;br&gt;Would make a number of changes to the Pharmacy Practice Act and Uniform Controlled Substance Act, including:&lt;br&gt;(1) pharmacies registered with the DEA and in which controlled substances are stored or dispensed must complete a controlled-substances inventory when there is a change in the pharmacist-in-charge, which must contain the information required in an annual inventory with copies to be maintained for a period of five years after it is completed; (2) Would provide a definition of “emergency situation” (situation in which a prescribing practitioner determines that (a) immediate administration of the controlled substance is necessary for proper treatment of the patient; (b) no appropriate alternative treatment is available, including administration of a drug which is not a controlled substance listed in schedule II; and (c) it is not reasonably possible for the prescribing practitioner to provide a signed, written or electronic prescription to be presented to the person dispensing the controlled substance prior to dispensing; (3) Would require completion of a partially filled controlled schedule II controlled substance prescription to be completed no later than 30 days after the date on which the prescription is written; (4) Authorizes pro-re nata or PRN refills in providing information relating to the number of refills for a schedule III, IV or V controlled substance; (5) Would authorize, for multidrug containers, more than one drug, device, or biological to be dispensed in the same container when (a) the container is prepackaged by the manufacturer, packager, or distributor and shipped directly to the pharmacy in this manner or (b) the container does not accommodate greater than a thirty-one day supply of compatible dosage units and is labeled to identify each drug or biological in the container in addition to all other information required by law; (6) Would require use of the DEA number of the pharmacy at which prescriptions are filled to be contained on the prescription label in cases in which a pharmacy fills prescriptions for controlled substances on behalf of another pharmacy under contractual agreement or common ownership; (7) Would exempt pharmacist interns, pharmacy technicians, and pharmacy clerks selling hypodermic syringes or needles for the prevention of the spread of infectious diseases from provisions of law regarding delivery of drug paraphernalia to be used for injection of a controlled substance into the human body; (8) Would exempt pharmacist interns and pharmacy technicians from requirement to file a report of loss or theft of a controlled substance to the DEA; (9) Would exempt pharmacist interns and pharmacy technicians from having to report fellow professionals engaging in unprofessional conduct except for professionals practicing while their ability to practice is impaired by alcohol, controlled substances, or narcotic drugs; (10) Would require a pharmacist intern to be supervised at all times while performing functions of a pharmacist intern, which may include all aspects of the practice of pharmacy, unless otherwise restricted; (11) Would authorize a pharmacist to enter into a practice agreement with a licensed health care practitioner authorized to prescribe independently to provide pharmaceutical care according to written protocols; (12) Would allow the quantity of drug indicated in a medical order for a resident of a long-term care facility to be sixty days unless otherwise limited by the prescribing practitioner; (13) Would provide conditions under which the unused portion of a drug administered to a patient in a hospital may be provided upon discharge from the hospital for continued use in treatment of the patient; and (14) Would allow an emergency box to contain multiple dose vials.</td>
<td>Support</td>
<td>In Committee</td>
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<td><strong>LB 167</strong>&lt;br&gt;Senator Ebke&lt;br&gt;Judiciary Committee&lt;br&gt;Hearing 1/25/2017</td>
<td>Controlled Substances&lt;br&gt;Would include cannabidiol in a drug product approved by the federal Food and Drug Administration as a Schedule V controlled substance</td>
<td>Support</td>
<td>General File</td>
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<tr>
<td><strong>LB 223</strong>&lt;br&gt;Senator Kuehn&lt;br&gt;Health &amp; Human Services Committee&lt;br&gt;Hearing 3/23/2017</td>
<td>Prescription Drug Monitoring Program&lt;br&gt;Would make statewide health information exchange for access by participants if such access is in compliance with the privacy and security protections set forth in the provisions of the Health Insurance Portability and Accountability Act. Would require users accessing the prescription drug monitoring system to undergo training on proper usage of the prescription drug monitoring system.</td>
<td>Oppose &amp; Seek Amendments</td>
<td>In Committee</td>
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<td>LB 227</td>
<td>Senator Wishart Health &amp; Human Services Committee Hearing 2/3/2017</td>
<td>Brain Injury Trust Fund</td>
<td>Watch</td>
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<td>LB 267</td>
<td>Senator Linehan Health &amp; Human Services Committee Hearing 1/26/2017</td>
<td>Onsite Vaccinations</td>
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<td>LB 293</td>
<td>Senator Larson Judiciary Committee Hearing 1/25/2017</td>
<td>Controlled Substances Schedule</td>
<td>Watch</td>
<td>General File</td>
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<td>LB 296</td>
<td>Senator McCollister Judiciary Committee Hearing 1/26/2017</td>
<td>Pharmacist Immunity</td>
<td>Support</td>
<td>In Committee</td>
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### National Poison Prevention Week

**MARCH 19-25, 2017**

Poisoning is the #1 cause of injury-related death in the U.S.

The third week in March each year is designated as National Poison PRevention Week, a week dedicated to raising awareness about the burden of poisoning in the U.S. and highlighting specific ways to prevent it. Be prepared for poisoning emergencies by programming the Poison Help Line in your phone today, 1-800-222-1222!

#NPPW17 #PREVENTPOISON
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<tr>
<td>LB 324</td>
<td>Senator Kolterman</td>
<td>Banking, Commerce &amp; Insurance Committee</td>
<td>2/27/2017</td>
<td>Pharmacy Benefit Fairness and Transparency Act (1) Would require a pharmacy benefit manager to obtain a certificate of authority as a third-party administrator and be subject to the Third-Party Administrator Act and Pharmacy Benefit Fairness and Transparency Act; (2) Would require a pharmacy benefit manager, within seven days after price increase or decrease notification by a manufacturer, supplier, or nationally recognized source, to adjust its payment to the contacted pharmacy consistent with the price increase or decrease; (3) Would require a pharmacy benefit manager to accept into its network any pharmacy or pharmacist in good standing and prohibit exclusion of a Nebraska pharmacy from participation in its specialty pharmacy network, provided the pharmacy is willing to accept the terms of the pharmacy benefit manager's agreement with its specialty pharmacy's and prohibit requiring a pharmacy or pharmacy to participate in one contract with a pharmacy benefit manager in order to participate in other contracts with the same pharmacy benefit manager; (4) Would prohibit the charging of fees or higher co-pays by covered individuals who use a mail-order pharmacy in order to utilize a contracted pharmacy or to prohibit a pharmacist or contract pharmacy from mailing a prescription drug to a covered individual; (5) Would require a pharmacy benefit manager to make readily available to the Director of Insurance and to each contracted pharmacy information related to the pharmacy benefit manager's pricing methodology and reimbursement amount for single-source and multiple-source prescription drugs and compounds and specialty drugs; (6) Would require the reimbursement amount for prescription drugs to be updated no less than every seven days by the pharmacy benefit manager; (7) Would require all financial benefits (rebates, discounts, credits, fees, grants, chargeback's, or other payments or financial benefits of any other kind) the pharmacy benefit manager receives to be disclosed to the covered entity with which the pharmacy benefit manager contracts and to disclose to the covered entity and to the contracted pharmacy the method used to calculate total dispensing fees, the cost of the prescription drug, administrative fees, and any other fee payment; (8) Would prohibit a pharmacy benefit manager from charging contracted pharmacy's transaction-based or claims-processing fees; (9) Would require benefits payable under a pharmacy benefits management plan to be paid within 20 days after receipt of a clean claim, if submitted electronically, or 30 days after receipt, if the claim is submitted in paper format; (10) Would prohibit adjudication of a clean claim from being audited unless fraud is suspected and establishes the manner in which an audit of a contracted pharmacies records by a pharmacy benefit manager is to be conducted (two-weeks prior notice; conducted by or in consultation with a pharmacist employed by a pharmacy benefit manager; cover period not to exceed two years from the date on which the claim was submitted to or adjudication; not conducted during the first seven calendar days of any month and establish an appeals process); and (11) Would authorize sharing of information regarding the cost, price, or co-payment of prescription drug with a covered individual or covered individual's caregiver by a pharmacist or contracted pharmacy without being subject to penalties or removal from a network or plan.</td>
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<td>LB 368</td>
<td>Senator Lowe</td>
<td>Transportation Committee</td>
<td>2/6/2017</td>
<td>Repeal Motorcycle Helmet Law Would increase the motorcycle registration fee by $19 to be remitted to the State Treasurer for credit to the Motorcycle Safety and Brain Injury Trust Fund. Would (a) prohibit a person from operating a motorcycle or moped on any highway in Nebraska unless wearing eye protection (b) prohibit any person under the age of 8 years from being a passenger on a motorcycle or moped; and would exempt individuals at least 21 years of age from motorcycle helmet requirement.</td>
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<td>LB 402</td>
<td>Senator Hilkemann</td>
<td>Health &amp; Human Services Committee</td>
<td>2/15/2017</td>
<td>Nebraska Regulation of Health Professions Act Would change provisions of the Nebraska Regulation of Health Professions Act.</td>
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<td>Bill</td>
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<td>LB 420</td>
<td>Senator McCollister</td>
<td>Business &amp; Labor Committee</td>
<td>Hearing 3/13/2017</td>
<td>Fair Chance Hiring Act Would prohibit public and private employers and employment agencies from asking an applicant to disclose, orally or in writing, information concerning the applicant's criminal record or history, including any inquiries on any employment application, until the employer or employment agency has determined the applicant meets the minimum employment qualifications. Would apply to employers with 15 or more employees.</td>
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<td>LB 425</td>
<td>Senator Crawford</td>
<td>Health &amp; Human Services Committee</td>
<td>Hearing 1/27/2017</td>
<td>Nurse Practitioner Practice Act Would change and eliminate certain licensure requirements and permit practice without an integrated practice agreement for certain nurse practitioners.</td>
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<td>LB 438</td>
<td>Senator Howard</td>
<td>Revenue Committee</td>
<td>Hearing</td>
<td>Cigarette Tax Would increase cigarette and tobacco taxes as prescribed and provide for the distribution of funds.</td>
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<td>LB 441</td>
<td>Senator Morfeld</td>
<td>Health &amp; Human Services Committee</td>
<td>Hearing 3/8/2017</td>
<td>Medicaid Expansion Would change eligibility provisions under the Medical Assistance Act.</td>
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<td>LB 473</td>
<td>Senator Walz</td>
<td>Business &amp; Labor Committee</td>
<td>Hearing 3/13/2017</td>
<td>Mandated Employee Rest Periods 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>
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<td>LB 474</td>
<td>Senator Baker</td>
<td>Banking, Commerce &amp; Insurance Committee</td>
<td>Hearing 2/13/2017</td>
<td>Synchronized Medications 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 pro-rated daily cost-sharing for the beneficiary for fee paid for alignment services.</td>
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<td>LB 481</td>
<td>Senator Kuehn</td>
<td>Health &amp; Human Services Committee</td>
<td>Hearing 2/2/2017</td>
<td>Drug Product Selection Would authorize drug product selection for interchangeable, biological products in place of the brand-name drug or the biological product contained in a medical order of a practitioner. Would require a pharmacist receiving a prescription for a biological product who chooses to dispense an interchangeable biological product for the prescribed product, to advise the patient or the patient's caregiver the drug product selection has occurred and within three business days after dispensing a biological product, require the dispensing pharmacist or his or her designee to make an entry of the specific product provided to the patient, including the name of the product and the manufacturer. Would require communication of such dispensing to be conveyed by making an entry that is electronically accessible to the prescriber through an interoperable medical records system, electronic prescribing technology, a pharmacy benefit management system, or a pharmacy record. Would require the Department to maintain a link on its website to the current list of all biological products that the Federal Food and Drug Administration has determined to be interchangeable biological products.</td>
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<td>Bill</td>
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<td>LB 487</td>
<td>Senator Morfeld</td>
<td>Judiciary Committee</td>
<td>2/23/2017</td>
<td>Immunity for Drug Overdose Witnesses: Would provide exception to certain crimes for persons witnessing or experiencing drug overdoses and provide protection from civil liability for emergency responders and peace officers administering naloxone.</td>
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<tr>
<td>LB 563</td>
<td>Senator McCollister</td>
<td>Revenue Committee</td>
<td>Hearing</td>
<td>Sales Tax on Services/Elimination of Certain Sales and Use Tax Exemptions: Would impose a sales tax on services including newspapers, Laundromats, tele floral deliveries, sale of Nebraska lottery tickets, maintenance and repair services; personal care services; lawn care; gardening services, storage and moving services, taxi, limousine and other transportation services, coin-operated machines used for dry-cleaning or other laundry services; weight loss services, bail bonding services; wedding planning services shoe shine services; social escort services; personal instruction services; parking services and docking fees; investment advice; interior design services; custom meat slaughtering, cutting and wrapping; hunting or fishing guide services; swimming pool cleaning and maintenance services; debt counseling services; tax return preparation services.</td>
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<tr>
<td>LB 586</td>
<td>Senator Linehan</td>
<td>Health &amp; Human Services Committee</td>
<td>3/23/2017</td>
<td>Prescription Drug Monitoring Program: Would authorize a dispense or any licensed or registered health care profession designated by a dispense to act as an agent for the dispense for purposes of submitting or accessing data in the prescription drug monitoring system provided the designee is directly supervised by the dispense.</td>
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<tr>
<td>LB 622</td>
<td>Senator Wishart</td>
<td>Judiciary Committee</td>
<td>3/23/2017</td>
<td>Medical Cannabis Act: Would authorize the use of marijuana for medicinal purposes.</td>
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<td>LB 661</td>
<td>Senator Kuehn</td>
<td>Gov’t-Military &amp; Veterans Affairs Committee</td>
<td>2/9/2017</td>
<td>Confidentiality of Information Relating to Lethal Injection: 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>
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Nebraska’s Mandatory Reporting Laws for Health Care Professionals

Objectives
At the conclusion of this lesson, pharmacists and pharmacy technicians should be able to:
1. Determine when a mandatory report is required.
2. Identify forms to file a mandatory report.
3. Explain the terminology in the laws pertaining to mandatory reporting.

Introduction
Caring for patients, no matter in what setting, can be stressful. Pharmacists, pharmacist interns, and pharmacy technicians may find another source of stress that is more difficult to manage: the stress of wondering if a mandatory report is required because of a situation they have just experienced. The goals of this lesson are to provide the Nebraska requirements and to help with some of this decision. In the end, only the pharmacist, pharmacist intern, or pharmacy technician will be able to decide what to do.

While stressful for the health care professional, the basis of having a mandatory reporting requirement is to protect the public. Mandatory reporting allows state officials to be alerted to problem practice more quickly and allows for a faster response. Focusing on public protection helps to ease some of the discomfort of participating in the process.

Nebraska Laws
Nebraska Revised Statute
§38-1,124
(1) The department shall enforce the Uniform Credentialing Act and for that purpose shall make necessary investigations. Every credential holder and every member of a board shall furnish the department such evidence as he or she may have relative to any alleged violation which is being investigated. (2) Every credential holder shall report to the department the name of every person without a credential that he or she has reason to believe is engaged in practicing any profession or operating any business for which a credential is required by the Uniform Credentialing Act. The department may, along with the Attorney General and other law enforcement agencies, investigate such reports or other complaints of unauthorized practice. The director, with the recommendation of the appropriate board may issue an order to cease and desist the unauthorized practice of such profession or the unauthorized operation of such business as a measure to obtain compliance with the applicable credentialing requirements by the person prior to referral of the matter to the Attorney General for action. Practice of such profession or operation of such business without a credential after receiving a cease and desist order is a Class III felony.

(3) Any credential holder who is required to file a report of loss or theft of a controlled substance to the Federal Drug Enforcement Administration shall provide a copy of such report to the department.
This section of law places an onus on all credentialed people. Even if exempted from other sections of the mandatory reporting laws, no one is exempt from the three mandates in this section. Everyone with a credential issued by the Department of Health and Human Services (Department) must do the following:

Section A. Furnish the department with any evidence he or she may have relative to any investigation;

Section B. Report the name of anyone who appears to be practicing without a credential when a credential is required;

Section C. Report the loss or theft of controlled substances to the DEA and the Department.

Section A Meeting these requirements isn’t difficult. If an investigator from the Department appropriately identifies herself/himself and asks for information, you should, to the best of your ability provide that information. You should not respond to someone you do not know until you are able to verify that the person asking for information has a right to that information. You do have the right to have a witness or even legal counsel with you at all interviews.

Section B If you believe someone is practicing without a credential, you must report that person to the Department. This may be someone who is feigning a license, who has had a credential revoked, or even a pharmacy technician who hasn’t met the certification requirements after January 1, 2017. Whether or not the person who is practicing without a credential is intentionally misleading people or simply forgot to renew a credential or attain a secondary credential, you are required to report if you know or have reason to know that someone is practicing without a credential. It is also reasonable to expect that credentialed people will verify the credentials of people they are working with and supervising using the Department of Health website https://www.nebraska.gov/LISSearch/search.cgi or check for a valid card.

Section C Reporting the loss or theft of controlled substances is a very circumscribed process – sending a copy of the report to the Department of Health and Human Services should not pose a hardship because the same DEA Form 106 submitted to the DEA may be copied and submitted to the Department. Even if you submit online to the DEA, print a copy to send to the Department, and keep a copy for your records. Additionally, reporting to both agencies keeps the credentialed person in compliance with the law.

Nebraska Revised Statute §38-1,125

(1) Every credential holder, except pharmacist interns and pharmacy technicians, shall, within thirty days of an occurrence described in this subsection, report to the department in such manner and form as the department may require whenever he or she:

(a) Has first-hand knowledge of facts giving him or her reason to believe that any person in his or her profession:

(1) Has acted with gross incompetence or gross negligence;

(2) Has engaged in a pattern of incompetent or negligent conduct, as defined in section 38-177; [A continued course of incompetent or negligent conduct in performing the duties of the profession.]

(iii) Has engaged in unprofessional conduct as defined in section 38-179; [See Section 38-179 at the end of this article]

(iv) Has been practicing while his or her ability to practice is impaired by alcohol, controlled substances, mind-altering substances, or physical, mental, or emotional disability; or

(v) Has otherwise violated the regulatory provisions governing the practice of the profession;

(b) Has first-hand knowledge of facts giving him or her reason to believe that any person in another profession:

(1) Has acted with gross incompetence or gross negligence; or

(2) Has been practicing while his or her ability to practice is impaired by alcohol, controlled substances, mind-altering substances, or physical, mental, or emotional disability; or

(c) Has been the subject of any of the following actions:

(i) Loss of privileges in a hospital or other health care facility due to alleged incompetence, negligence, unethical or unprofessional conduct, or physical, mental, or chemical impairment;

(ii) Loss of employment due to alleged incompetence, negligence, unethical or unprofessional conduct, or physical, mental, or chemical impairment;

(iii) An adverse judgment, settlement, or award arising out of a professional liability claim, including a settlement made prior to suit in which the consumer releases any professional liability claim against the credentialed person, or adverse action by an insurance company affecting professional liability coverage. The department may define what constitutes a settlement that would be reportable when a credential holder refunds or reduces a fee or makes no charge for reasons related to a consumer complaint other than costs;

(iv) Denial of a credential or other form of authorization to practice by any jurisdiction due to alleged incompetence, negligence, unethical or unprofessional conduct, or physical, mental, or chemical impairment;

(v) Disciplinary action against any credential or other form of permit he or she holds taken by any jurisdiction due to alleged incompetence, negligence, unethical or unprofessional conduct, or physical, mental, or chemical impairment;

(vi) Loss of membership in, or discipline of a credential related to the applicable profession by, a professional organization due to alleged incompetence, negligence, unethical or unprofessional conduct, or physical, mental, or chemical impairment; or

(vii) Conviction of any misdemeanor or felony in this or any other jurisdiction.
Continuing Pharmacy Education Lesson #2

(2) The requirement to file a report under subdivision (1)(a) or (b) of this section shall not apply:

(a) To the spouse of the credential holder;
(b) To a practitioner who is providing treatment to such credential holder in a practitioner-consumer relationship concerning information obtained or discovered in the course of treatment unless the treating practitioner determines that the condition of the credential holder may be of a nature which constitutes a danger to the public health and safety by the credential holder's continued practice; or
(c) When a credential holder who is chemically impaired enters the Licensee Assistance Program authorized by section 38-175 except as otherwise provided in such section.

(3) A report submitted by a professional liability insurance company on behalf of a credential holder within the thirty-day period prescribed in subsection (1) of this section shall be sufficient to satisfy the credential holder's reporting requirement under subsection (1) of this section.

Nebraska Revised Statute §38-2897

A pharmacy technician shall report first-hand knowledge of facts giving him her reason to believe that any person in his or her profession, or any person in another profession under the regulatory provisions of the department, may be practicing while his or her ability to practice is impaired by alcohol, controlled substances, or narcotic drugs. A report made to the department under this section shall be confidential. Any person making a report to the department under this section, except for those self-reporting, shall be completely immune from criminal or civil liability of any nature, whether direct or derivative, for filing a report or for disclosure of documents, records, or other information to the department under this section. The immunity granted by this section shall not apply to any person causing damage or injury by his or her willful, wanton, or grossly negligent act of commission or omission.

To start to understand all of the requirements in this section of law, the pharmacist, pharmacist intern, or pharmacy technician needs to understand the definitions of many of the terms used. While pharmacist interns and pharmacy technicians are not mandated to report under this section, there is never a prohibition against reporting. Learning the terminology will help the pharmacist intern and pharmacy technician either file a report or start a discussion with the supervising pharmacist. Statutory definitions are important information, but the statute does not contain definitions of the following terms and understanding them is essential to determining if a report must be filed.

First-Hand Information

This means that you are personally involved in something and gather the information using your basic senses – you heard someone, you smelled someone's breath, you spoke to someone or saw someone do something that is prohibited or untoward. Other professionals will find the following more helpful: “Firsthand experiences produce primary data.”

Gross Incompetence

This term is difficult. Incompetence is a lack of skill or ability to do something correctly or well. The term incompetence may also mean failure to meet a standard of performance. To rise to the level of gross incompetence the observer (the person with first-hand information) must believe that the lack of skill or failure to meet a standard is a “total failure” or an “utter ignoring of standards.” There is no standard measure for this distinction, but a possible decision making tool is, “Was this act or omission so obvious or conspicuous that I believe anyone seeing, hearing, smelling, or experiencing the same situation would agree with me?”

Gross Negligence

This term, as with the term gross incompetence, requires that the observer determine that a sufficient degree of negligence occurred to rise to the level of gross negligence. While incompetence means that the professional is unable to do something correctly, negligence means that the professional is able to perform a task or make a decision and simply doesn’t. Negligence may mean failing to provide care, failing to protect someone, or through other act or omission causing harm.

Impaired Practice

Another undefined term requiring judgment is “impaired practice.” The observer must determine that the professional would have performed tasks or functions differently or made different decisions in the absence of the impairment. Nebraska Revised Statute §38-1,125 of the statute goes on to say that the impairment may be caused by alcohol, controlled substances or mind altering substances, or physical, mental, or emotional disability.

Misdemeanor

Misdemeanors are typically crimes with a maximum punishment of 1-year incarceration or monetary fine or both.

Felony

A felony is a crime of a graver or more atrocious nature than those designated as misdemeanors; generally a crime punishable by death or imprisonment in a penitentiary for greater than 1-year or monetary fine or both. Even with definitions to help explain the statute, this lengthy section is most easily understood if it is broken into the three sub-sections of Section 1. Additionally, this section applies only to people who are currently credentialed. Non-credentialed practice or “practice without a license,” is covered by Nebraska Revised Statute §38-1,124(2) as previously discussed.

Reporting

Reporting someone in your profession

Nebraska Revised Statute §38-1,125(1)(a)

This subsection is crafted to require that credentialed people know more about their own profession than another profession. It is reasonable that a professional will understand the standards of care within her or his own profession more completely than the standards of care for another profession. Credentialed health care professionals in Nebraska are required to report the following first-hand experience with a member of their own profession.

i. Has acted, or failed to act, with either gross incompetence or gross negligence;
ii. Has a pattern of incompetent or negligent conduct;
iii. Has engaged in unprofessional conduct;
iv. Has practiced while impaired; or
v. Has violated a statute or regulation governing that profession.

Reporting someone in another profession Nebraska Revised Statute §38-1,125(1)(b)
Credentialed health care professionals are required to report other credentialed health care professionals from a different profession only when gross incompetence, gross negligence or impaired practice are evident.

Reporting yourself Nebraska Revised Statute §38-1,125(1)(c)
The final requirement of this section is the requirement that credentialed people report themselves to the Department for any of the following:
i. Loss of privileges at a facility due to allegations of incompetence, negligence, unethical behavior, unprofessional conduct, impaired practice, or a voluntary limitation of privileges or resignation while under investigation or evaluation for any of these.
ii. Being fired for anything listed in i.
iii. Losing a case or settling a case for claimed professional liability.
iv. Being denied a credential in any other state or jurisdiction.
v. Discipline against a credential in any other state or jurisdiction.
vi. Losing membership in a professional organization for any of the reasons listed in i.
vii. Conviction of any misdemeanor or felony in Nebraska or in any other state or jurisdiction.

Exemptions
There are exemptions from the mandatory reporting statutes and there are allowances to reduce paperwork. It is important to understand if the situation under consideration is exempted from reporting or not.

Un-credentialed practice and loss/theft of controlled substances are NOT exempted for anyone for any reason. Even spousal privilege has not been applied to reporting these instances.

Pharmacist Interns and Pharmacy Technicians have been exempted from reporting under Nebraska Revised Statute §38-1,125. They are not prohibited from reporting, but they have no statutory duty to do so. It is important to note that Nebraska Revised Statute §38-2897 immediately removes the exemption for pharmacy technicians in reporting impaired practice listed in Nebraska Revised Statute §38-1,125. Pharmacy Technicians are required to report impaired practice, as are pharmacists. Only pharmacist interns are exempted from reporting impaired practice.

If you are providing health care to a practitioner and have a practitioner-consumer relationship you may be exempt from reporting. If, however, you determine that the condition of your patient is a danger to the public, you may still need to report. Licensee Assistance Programs are not required to report when a credentialed person enters the program.

You are not required to report yourself when your professional liability insurance company has reported an adverse claim or settlement on your behalf.

Peer review committees and committee members are not required to report when the source of first-hand information is committee service.

If you can’t decide, you should report
When deciding to file a report or not, the pharmacist, pharmacist intern, or pharmacy technician should apply the requirements of the law to the best of her/his ability. If you are unable to decide – report. When you are involved in an event that makes you question whether you should report, it is likely of sufficient concern for public safety that you would choose to report. Reporting, first and foremost, is a way to protect the public from sub-standard or unethical practice. Reporting is also important for protecting your own credential. Not reporting, because of confusion, is not worth losing your credential. The best advice is, “When in doubt – report.” It is also important to note that an exemption from reporting does not apply to providing accurate and complete information on applications for a new or renewal credential. While the pharmacist intern or pharmacy technician may be exempted from self-reporting, that same person will have to disclose misdemeanor and felony convictions at the time of application.

If you are unsure if you need to report under the misdemeanor and felony conviction requirement, you should make every effort to determine the nature of your conviction or conviction. Again, when in doubt – report. The concept of misdemeanor and felony is difficult for many people. In general traffic citations – failure to yield, speeding – are not mandatorily reported. Other convictions are not as easily described, as they can vary from city to city or jurisdiction to jurisdiction. For a time, watering your lawn on the wrong day in Lincoln was a misdemeanor, but watering your lawn on the wrong day in Omaha was not. When in doubt – report.

Reporting
There are several ways to meet the reporting requirements. Using the Nebraska Department of Health & Human Services website, locate “Licensing and Registrations” (http://dhhs.ne.gov/ Pages/licensing.aspx) in the left column locate Rules & Regulations. From this page locate Title 172 – Professional and Occupational Licensure. Chapter 5 is Mandatory Reporting (http://www sos.ne.gov/rules-and-reg/ research/Rules/Health_and_Human_Services_System/Title-172/ Chapter-005.pdf). At the end of the chapter you will find the attachments that are the reporting forms. NOTE: The address on the attachments is not accurate and your mail will be returned. You may also access mandatory reporting forms at: http:// dhhs.ne.gov/Pages/reg_invest-p.aspx#Forms. The address for submitting reports on this page is functional. Additionally, this site allows you to submit forms online. If you do not know the information asked, you may leave these sections blank, e.g. another professional’s home address or birthdate.

Representatives of the Department will assist you with questions or confusion in filling out reports. Contact information can be found at http://dhhs.ne.gov/Pages/ reg_invest-p.aspx.

Conclusion
While people credentialed by the Department may have a duty to report other circumstances (child abuse, elder abuse, etc) the duty to report a colleague or oneself is a challenge most hope to avoid.
Continuing Pharmacy Education Lesson #2

Being faced with the decision to report a colleague or yourself is difficult. Knowing what must be reported and being able to access the necessary forms to complete the report is essential to practicing your profession, whether you are a pharmacist, a pharmacist intern or a pharmacy technician. This lesson has provided information to assist in making decisions and locating resources. The final reporting decision lies with the credentialed person.

References
Nebraska Revised Statutes 2016
Misdemeanor watering convictions could mean trouble down the road, Lincoln Journal Star, Nancy Hicks, 4 Sep 2012.

Unprofessional Conduct as Defined in Nebraska Revised Statute §38-179
Unprofessional conduct means any departure from or failure to conform to the standards of acceptable and prevailing practice of a profession, regardless of whether a person, consumer, or entity is injured, or conduct that is likely to deceive or defraud the public or is detrimental to the public interest, including but not limited to:
1. Receipt of fees on the assurance that an incurable disease can be permanently cured;
2. Division of fees, or agreeing to split or divide the fees, received for professional services with any person for bringing or referring a consumer other than (a) with a partner or employee of the applicant or credential holder or his or her office or clinic, (b) with a landlord of the applicant or credential holder pursuant to a written agreement that provides for payment of rent based on gross receipts, (c) with a former partner or employee of the applicant or credential holder based on a retirement plan or separation agreement, or (d) by a person credentialed pursuant to the Water Well Standards and Contractors’ Practice Act;
3. Obtaining any fee for professional services by fraud, deceit, or misrepresentation, including, but not limited to, falsification of third-party claim documents;
4. Cheating on or attempting to subvert the credentialing examination;
5. Assisting in the care or treatment of a consumer without the consent of such consumer or his or her legal representative;
6. Use of any letters, words, or terms, either as a prefix, affix, or suffix, on stationery, in advertisements, or otherwise, indicating that such person is entitled to practice a profession for which he or she is not credentialed;
7. Performing, procuring, or aiding and abetting in the performance or procurement of a criminal abortion;
8. Knowingly disclosing confidential information except as otherwise permitted by law;
9. Commission of any act of sexual abuse, misconduct, or exploitation related to the practice of the profession of the applicant or credential holder;
10. Failure to keep and maintain adequate records of treatment or service;
11. Prescribing, administering, distributing, dispensing, giving, or selling any controlled substance or other drug recognized as addictive or dangerous for other than a medically accepted therapeutic purpose;
12. Prescribing any controlled substance to (a) oneself or (b) except in the case of a medical emergency (i) one's spouse, (ii) one’s child, (iii) one’s parent, (iv) one’s sibling, or (v) any other person living in the same household as the prescriber;
13. Failure to comply with any federal, state, or municipal law, ordinance, rule, or regulation that pertains to the applicable profession;
14. Disruptive behavior, whether verbal or physical, which interferes with consumer care or could reasonably be expected to interfere with such care; and
15. Such other acts as may be defined in rules and regulations. Nothing in this section shall be construed to exclude determination of additional conduct that is unprofessional by adjudication in individual contested cases.

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 2017 Membership Year must be received by December 11, 2017. 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 2017 will be sent to NABP e-Profiles before July 15, 2017.

The Nebraska Council for Continuing Pharmacy Education (NCCPE) is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education (CPE). This CPE home study lesson has been accredited for 1.0 contact hour or 0.10 CEU. UAN 0128-0000-17-013-H03-P for pharmacists and 0128-0000-17-013-H03-T for pharmacy technicians. This lesson is a knowledge-based CPE activity targeted to pharmacists and pharmacy technicians.

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

Quiz Answers may be submitted:
1. Online: www.npharm.org
2. Fax: 402-420-1406
3. Email: m&p@npharm.org
4. Mail: NPA Mortar & Pestle
   6221 S 58th St, Ste A
   Lincoln, NE 68516
Nebraska’s Mandatory Reporting Laws for Health Care Professionals
Quiz #2, February 2017, ACPE #0128-0000-17-013-H03-P/T

1. A pharmacist smells alcohol on the breath of a fellow pharmacist and notices that she has made an error. Which of the following is/are true about the observing pharmacist?
   a. A mandatory report of a person in your profession is required
   b. A mandatory self-report is required
   c. A mandatory report of a person in your profession may be required
   d. The observing pharmacist should call the LAP

2. Unprofessional conduct is generally described as?
   a. Harming a patient
   b. Failure to conform to the standards of the profession
   c. Having to look up a dose
   d. Not wearing a name tag while on duty

3. What is the time limit for filing a mandatory report?
   a. 3 days
   b. 10 days
   c. 15 days
   d. 30 days

4. Which of the following is not considered first-hand information?
   a. You see a technician place a tablet in his pocket
   b. You smell alcohol on the breath of a colleague
   c. You read a quality assurance report describing an error
   d. You heard a physician yell at a nurse

5. There are 3 mandates for all credentialed people listed in Nebraska Revised Statute §38-1,124. Which is not correct?
   a. All credentialed people must report practice by un-credentialed people
   b. All credentialed people must cooperate with investigators from the Department
   c. All credentialed people must report a loss or theft of controlled substances
   d. Each of these is correct, there is no incorrect answer listed

6. What steps should a pharmacist take to verify that a pharmacy technician is properly credentialed?
   a. Check the Department website for the technician’s name and credential
   b. Ask to see the wallet card issued by the Department
   c. Look at a certification document issued by a certifying body
   d. A and B are correct

7. If you observe something concerning, but it is not defined in Nebraska Revised Statute §38-179, are you still allowed to report?
   a. No, you may only report things listed in the statute
   b. Yes, mandatory reporting always applies
   c. Yes, you may report anything. You MUST report those events listed as mandatorily reportable
   d. No, you could be charged with slander if you report

8. Mandatory Reporting Laws in Nebraska do not apply to pharmacy technicians.
   a. True  b. False

9. If a pharmacy technician is convicted of a misdemeanor, he/she must report himself/herself within 30 days.
   a. True  b. False

10. Pharmacy technicians may only report those events that he/she is required to report.
    a. True  b. False

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 11, 2017

Circle one (1) Answer:

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

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.

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Our Mission
To help our customers attain peace of mind through specialized insurance products, risk management solutions, and superior personal service.
To paraphrase John Godfrey Saxe; laws are like sausages, it's better not to see them being made. I am not an expert on sausages, but I would disagree with this comment with regards to laws. Even if we don’t get involved in the making of laws, we will be subject to them nonetheless. Pharmacists can ill afford to be impacted by laws drafted by those who know nothing about pharmacy.

Unfortunately for many of us, lobbying is a word with very negative connotations. It projects images of under the table dealings and improper exchanges of cash. So how do we inform lawmakers of the impact of proposed laws on the practice of pharmacy? Through advocacy.

Advocacy is simply the act of supporting a cause, an idea, or a proposed policy. Many state and national associations organize advocacy meetings for their members. While we can all do this individually, a group of concerned citizens visiting the lawmaker’s office together can certainly make a larger impact. The purpose of these visits is to educate the lawmaker and their staff on proposed laws that impact our profession. We might be in favor of a proposal, opposed to it or want to amend the language as presented.

Lawmakers are serving because they want to make a positive difference in our society. However, they are not experts in every field. There is only one pharmacist, Buddy Carter of Georgia, in the 114th Congress. The other Senators and Representatives need pharmacists’ help to understand how proposals will affect pharmacy practice.

I have participated in advocacy meetings on both the state and national level. In my experience, the lawmakers and staffers are eager to hear how proposals will affect constituents in their districts. The meetings usually consist of an introduction, explanation of why you are there, what the real impact in their district will be, and what action you want them to take. For pharmacists, the potential impact is not always direct. The impact may be on our patients; denying access, increasing costs, or creating hurdles to care. Of course, these indirect impacts will have an impact on your pharmacy practice. Many times the true impact on patients is not readily apparent. Pharmacists can explain how a particular policy will make it more difficult for patients to get their medications. Don’t expect immediate action. It is always a pleasant surprise to get a commitment, but many times the materials that you provide are circulated in the office before decisions are made.

Not all advocacy has to take place in Washington, D.C. or your state capital. Invite your lawmaker to visit your pharmacy while they are home in the district. Then they will get to see first-hand what you are doing for your patients, their constituents. You can also advise them about how proposed laws will impact your ability to provide these services. First-hand knowledge and stories of real impacts (not just theoretical ones) will have the most influence on the process.

If pharmacists don’t educate lawmakers about the effects of the changes on their practices and their patients, who will? Don’t think of it as lobbying. We are really educating our lawmakers. Joining and participating in professional organizations is a good way to get started. In the end, the profession will benefit and ultimately, our patients will too.
New Drugs: Nuplazid, Anthim, and Venclexta

This CPE lesson was written by Abby Grieser, PharmD Candidate, University of Nebraska Medical Center College of Pharmacy, who does not have any conflicts of interest, nor does she have financial relationships with a commercial interest related to this activity.

**Objectives**

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

1. Identify the indication, dosage, therapeutic class, and pharmacologic action for each new drug.
2. Describe significant adverse effects, drug interactions, warnings, cautions, and important patient counseling information for each new drug.

**Nuplazid™ (pimavanserin)**

**Introduction**

Parkinson's disease (PD) is a progressive neurological disorder that affects movement. An estimated 0.3% of the population in industrialized countries is affected by PD. Patients with PD lack a sufficient amount of dopamine in the brain leading to motor disturbances. These motor disturbances include tremors of the extremities and face, bradykinesia, rigidity and stiffness of the limbs and trunk, and impaired balance.

As the disease progresses, patients begin to experience psychotic symptoms including visual hallucinations and delusions. Parkinson's disease psychosis (PDP) is prevalent in more than 30% of patients with PD and is linked to an estimated 24% of PD related hospitalizations. PDP leads to reduction in both patient and caregiver quality of life.

Medications used to treat PD motor symptoms are thought to contribute to PDP symptoms. Removing or reducing PD medications is one method of managing PDP symptoms, although this usually leads to worsening and often times unmanageable motor symptoms. In general, antipsychotic medications are avoided in the treatment of PDP because they work as antagonists at the D2 receptor, blocking dopamine and leading to worsening motor function. Currently, only two antipsychotic medications are used for the treatment of PDP, quetiapine and clozapine, both with inconsistent results. Pimavanserin offers a new antipsychotic therapy option for the treatment of PDP.

**Indication**

Pimavanserin is indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.

**Mechanism of Action**

Pimavanserin is a combination inverse agonist and antagonist primarily at serotonin 5HT2A receptors, and to a lesser extent 5HT2C receptors. The exact mechanism of pimvanserin in the treatment of PDP associated hallucinations and delusions is unknown. Unlike other atypical antipsychotics, pimavanserin does not have dopamine blocking activity. The lack of dopamine activity allows the drug to treat Parkinson's disease psychosis without worsening motor symptoms.

**Dosage**

The recommended daily dose for pimavanserin is 34 mg given by mouth once daily in two 17 mg tablets. Dose titration is not required upon initiation or discontinuation. This medication can be taken with or without food.

When co-administered with a strong CYP3A4 inhibitor the dose of pimavanserin should be reduced to 17 mg once daily. No empiric dosage adjustments are recommended when being co-administered with strong CYP3A4 inducers, but patients should be monitored for reduced efficacy.

**Safety and Efficacy**

A randomized, double blind, placebo controlled, parallel-group study was conducted on 199 patients to evaluate the safety and efficacy of pimavanserin therapy in patients with PDP. Patients were randomized in a one-to-one ratio to receive either pimavanserin 34 mg or placebo once daily. All patients had a diagnosis of Parkinson’s disease for at least one year and presented with psychotic symptoms. Efficacy was evaluated using the PD-adapted Scale for the Assessment of Positive Symptoms (SAPS-PD). It is a 9-item scale scored from 0-5 with 0 being no symptoms and 5 representing severe and frequent symptoms. SAPS-PD scores were taken at baseline and six weeks after entering the study. Pimavanserin 34 mg was proven to be statistically significantly superior to placebo in decreasing frequency and/or severity of hallucinations and delusions in patients with PDP. Average baseline SAPS-PD scores were decreased by a mean of 5.79 in the pimavanserin 34 mg group, as compared to a mean decrease of 2.73 in the
placebo group. Additionally, pimavanserin showed no evidence of effect on motor function when compared to placebo.6 Safety was assessed by looking at the percentage of adverse reactions that occurred during the randomized controlled trials. A total of 8% (16/202) of pimavanserin 34 mg treated patients experienced adverse reactions and discontinued treatment. This is compared to a total of 4% (10/231) of placebo treated patients that discontinued treatment due to adverse reactions. Based on the evidence from the clinical trials, there is no common pathological mechanism that links these adverse events together. Other approved atypical-antipsychotic drugs have similar adverse reaction profiles and similar rates of occurrence.6

Common Side Effects
Common adverse reactions of pimavanserin include peripheral edema (7% incidence), confusional state (6%), nausea (7%), hallucinations (5%), constipation (4%), and gait disturbances (2%).2 Other adverse reactions reported were urinary tract infections and fatigue.2

Contraindications and Warnings
Pimavanserin has a boxed warning for increased mortality in elderly patients with dementia-related psychosis. All atypical antipsychotics have this black box warning. Elderly patients with dementia-related psychosis are at an increased risk of death when being treated with antipsychotic drugs. Analysis of 17 dementia-related psychosis placebo-controlled trials shows a 1.6 to 1.7 times increased risk of death in elderly dementia patients who are being treated with atypical antipsychotic medication.5

Pimavanserin has also been shown to prolong the QTc interval. Patients with a history of QTc prolongation should avoid the use of pimavanserin. Pimavanserin should also be avoided in patients with a history of cardiac arrhythmias and in patients who have conditions that increase the risk of torsades de pointes including bradycardia, hypokalemia, and hypomagnesaemia. Patients taking other medications that prolong the QTc interval should not take pimavanserin.5

Patients who have impaired renal function with a creatinine clearance of ≤30 mL/min should avoid the use of this medication. Pimavanserin should also be avoided in patients with hepatic impairment, as it has not been studied in this population.5

Drug-Drug Interactions
The use of pimavanserin should be avoided in patients who are taking medications known to prolong the QTc interval. This includes class 1A antiarrhythmics, class 3 antiarrhythmics, ziprasidone, chlorpromazine, thioridazine, and certain antibiotics (moxifloxacin, gatifloxacin, clarithromycin).5

Pimavanserin is metabolized by CYP3A4. Because of this, dosing adjustments and monitoring are needed when pimavanserin is co-administered with CYP3A4 inhibitors (See Dosage).5

Monitoring Parameters
Patients taking pimavanserin should be monitored for changes in neurological function. Routine labs should also be drawn including liver function tests, serum creatinine, and serum electrolytes.5

Anthim™ (Obiltoxaximab)
Introduction
Anthrax is an infectious disease caused by the organism Bacillus anthracis. B. anthracis is a bacteria that occurs naturally in the soil and affects both domestic and wild animals. Most humans become exposed to anthrax through contact with animals or animal products such as hides or wool.7 Anthrax is not contagious in humans, so it cannot be spread from person to person like a cold or influenza. Humans become infected when B. anthracis spores enter the body. Spores can enter the body through ingestion of contaminated food or water, inhalation of spores, or through a cut or scrape. Once spores have entered the body they can become activated into anthrax bacteria. After becoming activated the bacteria multiplies, producing toxins and poisons.8

Symptoms of anthrax vary depending upon the route of infection. Cutaneous anthrax presents as a group of small bumps or blisters that develop into a painless skin ulcer with a black center. Inhalational anthrax symptoms include fever and chills, chest discomfort and shortness of breath, confusion or dizziness, nausea, vomiting, stomach pains, drenching sweats, and body aches. Patients who are exposed to ingested anthrax may present with fever and chills, swelling of the neck or glands, sore throat, nausea or vomiting, bloody diarrhea, flushing of the face, stomach pain, and swelling of the abdomen.9

The use of inhalational anthrax as a bioterrorism weapon has been a concern in industrialized nations. Due to this concern, most hospitals and emergency response teams need a plan in place to treat those that have become exposed to anthrax. In the past, the only way to treat those infected with anthrax was through antibiotics, mainly ciprofloxacin.10 Obiltoxaximab offers an alternative to treatment as an adjunct to antibiotics, or alone in those that cannot be treated with antibiotics.

Indications
Obiltoxaximab is indicated in adult and pediatric patients for the treatment of inhalational anthrax due to B. anthracis in combination with appropriate antibacterial drugs. Anthim is also indicated for prophylaxis of inhalational anthrax when alternative therapies are not appropriate or available.11

Mechanism of Action
Obiltoxaximab is a monoclonal antibody that binds to the protective antigen (PA) of Bacillus anthracis toxin. Obiltoxaximab works by blocking the enzymatic toxin components responsible for the pathogenic effects of anthrax by preventing the entry of anthrax lethal factor and edema factor into the cells.11

Dosing and Administration
Premedication with diphenhydramine is recommended before administering obiltoxaximab. Obiltoxaximab should be administered intravenously over 90
minutes as a one-time dose. Dosing of this medication is weight-based. Patients weighing less than or equal to 15 kg should receive 32 mg/kg, patients weighing greater than 15 kg to 40 kg should receive 24 mg/kg, and patients weighing greater than 40 kg should receive 16 mg/kg. The injection is diluted in 0.9% sodium chloride before administration. Total volume of infusion is also weight-based (See Table 1).11

Vials should be visually inspected prior to use to ensure the solution does not contain any particles. Vials should be kept in their cartons until they are ready to be used in order to protect obiltoxaximab from exposure to light. Do not shake the vials. Obiltoxaximab should be administered immediately after dilution with 0.9% sodium chloride in a syringe. If the infusion is diluted in an IV infusion bag it may be stored at room temperature or in the refrigerator for 4 hours.11

Safety and Efficacy
The safety and efficacy of obiltoxaximab were evaluated in both healthy human subjects and animals, as it is not ethical to expose humans to inhalational anthrax. Three clinical trials involving a total of 320 subjects were conducted to test the safety of obiltoxaximab use in humans. Patients were given one or more 16 mg/kg IV doses of obiltoxaximab. Treatment was discontinued in 2.5% of patients (8/320) due to adverse reactions, including hypersensitivity reactions.11

Studies assessing the efficacy of obiltoxaximab were conducted on New Zealand White (NZW) rabbits and cynomolgus macaque monkeys. Animals were exposed to aerosolized B. anthracis at a level that would achieve 100% mortality if not treated. In trials assessing the prophylaxis efficacy of obiltoxaximab, the drug was administered before the development of symptoms. In trials assessing the treatment efficacy of obiltoxaximab, animals were given the drug after a positive serum electrochemiluminescence assay for B. anthracis protective antigen (PA) at a mean time of 30-40 hours post exposure. Animals were either treated with 16 mg/kg of obiltoxaximab or placebo. Treatment with obiltoxaximab resulted in significantly improved survival outcomes relative to treatment with placebo. Obiltoxaximab was also administered along with antibacterial agents, including levofloxacin, ciprofloxacin, and doxycycline. The combined administration of obiltoxaximab with antibacterial therapy resulted in higher survival outcomes than with antibacterial therapy alone.11

Common Side Effects
The most commonly reported side effects in patients given obiltoxaximab are headache, pruritis, infections of the upper respiratory tract, cough, vessel puncture site bruise, infusion site swelling, nasal congestion, infusion site pain, urticaria, and pain in extremities. The majority of these adverse reactions are related to hypersensitivity to obiltoxaximab.11

Contraindications and Warnings
Obiltoxaximab was issued a boxed warning for hypersensitivity reactions during medication infusion including anaphylaxis. Obiltoxaximab should only be administered under the close monitoring of a healthcare professional or other personnel trained to manage anaphylaxis. The infusion should be immediately stopped and the patient should be treated appropriately if hypersensitivity or anaphylaxis occurs. During safety trials, 10.6% (34/320) of patients experienced hypersensitivity reactions and 0.9% (3/320) of patients experienced anaphylaxis. Patients should be monitored for anaphylaxis for a short period after the infusion has been administered. Premedication with diphenhydramine is recommended and may help to prevent hypersensitivity reactions.11

Drug-Drug Interactions
There are no known drug interactions with obiltoxaximab.11

Monitoring Parameters
No laboratory monitoring is necessary. Patients should be closely monitored for hypersensitivity and anaphylaxis reactions during and after infusion of obiltoxaximab.11

Venclexta™ (venetoclax)
Introduction
Chronic lymphocytic leukemia (CLL) is a cancer affecting lymphocytes in the bone marrow. CLL usually progresses slowly over time, often with no symptoms for several years. Cancerous lymphocytes spread from the bone marrow into the bloodstream and cause extremely elevated white blood cell counts as CLL progresses. If untreated, CLL has the potential to spread to other parts of the body including the lymph nodes, liver, and spleen. There are several forms of CLL including B cell lymphocytic leukemia, prolymphocytic leukemia, large granular lymphocytic leukemia, and hairy cell leukemia.12

Certain CLL patients are affected by a deletion in the arm of chromosome 17, known as a 17p deletion.13 Patients with a 17p deletion have been shown to have worse outcomes than other CLL patients. These patients often have decreased response to standard treatment or they become resistant to treatment. Abnormalities involving chromosome 17 affect p53, a tumor-suppressing gene.15 Wild type p53 inactivates BCL-2, a protein that mediates cell survival.14,15 When a 17p deletion is present, the p53 gene can no longer inactivate BCL-2 and apoptosis of tumor cells decreases leading to increased cancer cell survival.14,15 The majority of CLL patients with a 17p deletion experience relapse or treatment resistance while on traditional therapies. Venetoclax offers an alternative therapy to 17p CLL patients that have become refractory to other treatments.4

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<tbody>
<tr>
<td>≤ 1 kg</td>
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<td>7 mL</td>
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**Indication**
Venetoclax is indicated for the treatment of CLL patients with a 17p deletion, as detected by an FDA approved test, and who have received at least one prior therapy.15

**Mechanism of Action**
Venetoclax is a small molecule inhibitor of BCL-2. BCL-2 is an anti-apoptotic protein that is related to prolonged tumor cell survival. Over-expression of BCL-2 in CLL patients has been shown to prevent tumor cell death and lead to increased resistance to chemotherapy. Venetoclax binds to the BCL-2 protein, restoring the processes of apoptosis by displacing pro-apoptotic proteins to trigger mitochondrial outer membrane permeabilization and the activation of capsases.15

<table>
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<tr>
<th>Table 2. Titration Schedule for Venetoclax15</th>
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<tr>
<td>Week</td>
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**Dosage**
Venetoclax is available in a 10 mg, 50 mg, and 100 mg oral tablet. It should be taken with a meal and water at approximately the same time each day. Venetoclax is titrated up weekly, over a period of 5 weeks to a maximum dose of 400 mg daily (see Table 2). Slow titration is required to reduce the potential of tumor lysis syndrome (TLS). A dose of 400 mg is then continued until CLL progresses or a toxicity develops.15

Dosing should be held or reduced if toxicities develop. These toxicities include blood chemistry changes, symptoms of TLS, neutropenia with infection and fever, and other grade 3 or 4 non-hematological toxicities. Specific recommendations exist based on event and occurrence of toxicity. Guidelines also exist for restarting venetoclax after dosing interruption (see Table 3). If dosing is interrupted during the titration phase the patient should remain on the reduced dose for 1 week before the next titration increase.15

<table>
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<th>Table 3. Restart Dose for Venetoclax After Dosing Interruption15</th>
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<tr>
<td>Dose at interruption</td>
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<td>400 mg</td>
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After the titration period is complete, if venetoclax is co-administered with strong CYP3A inhibitors the dose should be reduced by 75%. Using strong CYP3A inhibitors while venetoclax is still being titrated is contraindicated. Venetoclax dosing should be reduced by 50% when co-administered with moderate CYP3A inhibitors and P-glycoprotein inhibitors (P-gp).15

**Safety and Efficacy**
Safety and efficacy data for venetoclax is based on an open label, dose escalation trial in 116 patients with relapsed or refractory CLL or SLL. All patients received treatment. Patients were divided into two groups with 56 patients receiving dose escalation therapy starting at 20 mg or 50 mg, and then each patient was stepped up to 150 mg, 200 mg, 300 mg, 400 mg, 600 mg, 800 mg, and finally 1,200 mg. The other 60 patients received expansion therapy in which they were dose escalated to 400 mg daily and remained on that dose for the extent of the trial. The most clinically severe side effect seen in both groups was tumor lysis syndrome (TLS).16 TLS is a metabolic syndrome caused by the breakdown of malignant cells, leading to hyperuricemia, hyperphosphatemia, hyperkalemia, and hypocalcemia. If untreated these electrolyte imbalances cause kidney dysfunction, cardiac arrhythmias, seizures, and death.17 Approximately 18% (10/56) of patients on venetoclax had clinical or laboratory-only TLS, with only three patients presenting with clinical symptoms. Other serious adverse effects include febrile neutropenia, pneumonia, upper respiratory infection, and immune thrombocytopenia. The majority of the adverse effects were grade 1 or grade 2 and were usually self-limited nausea, diarrhea, or upper respiratory tract infections.16

Venetoclax was active in all doses that were studied and there were clinically significant reductions in CLL tumor burden. The overall response rate in the dose escalation cohort was 70% and the overall response rate in the expansion cohort was 82%. Patients taking venetoclax showed a median progression free survival of 25 months. At 15 months 75% of patients maintained a durable response.16

**Common Side Effects**
The common adverse effects of venetoclax are neutropenia, diarrhea, nausea, anemia, upper respiratory tract infection, thrombocytopenia, and fatigue. Other adverse effects reported include vomiting, constipation, peripheral edema, and headache.15

**Contraindications and Warnings**
Venetoclax should only be used in CLL patients with a known 17p deletion. Patients should be tested for a 17p deletion prior to initiation of therapy. Venetoclax may cause a rapid reduction in tumor burden which could lead to tumor lysis syndrome (TLS), particularly in the initial 5-week titration phase. All patients should be assessed for a risk of TLS prior to initiation of venetoclax. Patients should receive adequate hydration and anti-hyperuricemics during therapy to prevent TLS. A risk for neutropenia also exists in patients taking this medication. Patients should not receive live attenuated vaccines prior to, during, or after therapy. Venetoclax poses a risk to fetal development and all women of reproductive age should use proper contraception during therapy.15

**Drug-Drug Interactions**
The concomitant use of venetoclax with moderate CYP3A inhibitors, strong to moderate CYP3A inducers, P-gp inhibitors, and narrow therapeutic index P-gp substrates should be avoided. Medications in these categories alter the drug levels of venetoclax. If one of these medications must be co-administered with venetoclax, dosing adjustment is required (see Dosage). INR should be closely monitored when venetoclax is co-administered with warfarin.15
Monitoring Parameters
A pregnancy test should be given to all female patients of reproductive age prior to the start of treatment. All patients should be monitored for signs and symptoms of TLS and hematologic toxicities including a full CBC with differential and a radiographic CT scan to assess tumor burden. Serum electrolytes should be monitored along with uric acid levels and serum creatinine.15

References

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 2017 Membership Year must be received by December 11, 2017. 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 2017 will be sent to NABP e-Profiles before July 15, 2017.

Quiz Answers may be submitted:
1. Online: www.npharm.org
2. Fax: 402-420-1406
3. Email: m&p@npharm.org
4. Mail: NPA Mortar & Pestle
6221 S 58th St, Ste A
Lincoln, NE 68516
New Drugs: Nuplazid, Anthim, and Venclexta
Quiz #3, February 2017, ACPE #0128-0000-17-014-H01-P/T

1. Which receptor(s) does pimavanserin target?
   a. Dopamine
   b. Histamine
   c. Serotonin
   d. Both a and b

2. Pimavanserin has been approved to treat what condition?
   a. Bipolar disorder
   b. Manic depression
   c. Parkinson’s disease psychosis
   d. Schizophrenia

3. The use of pimavanserin can lead to what cardiologic condition?
   a. Atrial fibrillation
   b. Coronary artery disease
   c. Myocardial infarction
   d. QTc prolongation

4. When co-administered with a strong CYP3A4 inhibitor how should pimavanserin dosing be adjusted?
   a. Co-administration of a strong CYP3A4 inhibitor with pimavanserin is contraindicated
   b. No empiric dose adjustment is needed
   c. The dose should be increased to 51 mg daily
   d. The dose should be reduced to 17 mg daily

5. What is the approved indication for obiltoxaximab?
   a. Prophylaxis of inhalational anthrax
   b. Treatment of gastrointestinal anthrax in combination with antibacterial drugs
   c. Treatment of inhalational anthrax in combination with antibacterial drugs
   d. Both a and c

6. Obiltoxaximab has a boxed warning for which adverse effect?
   a. Anaphylaxis
   b. Angioedema
   c. Cardiovascular risk
   d. Stevens-Johnson Syndrome

7. Which drug class does obiltoxaximab belong to?
   a. Antibiotic
   b. Antiviral
   c. Monoclonal antibody
   d. Non-Steroidal Anti-inflammatory

8. Which drug metabolism and transport pathway(s) does venetoclax interact with?
   a. CYP2D6
   b. CYP3A
   c. P-gp
   d. Both b and c

9. What is the final maintenance dose for venetoclax?
   a. 100 mg once daily
   b. 200 mg twice daily
   c. 400 mg once daily
   d. 400 mg twice daily

10. What is the mechanism of action of venetoclax?
    a. Inhibits cell’s ability to disassemble microtubules
    b. Inhibits the enzyme dihydrofolate reductase
    c. Intercalates into DNA and inhibits topoisomerase II
    d. Small molecule inhibitor of BCL-2

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 11, 2017
New Name and Location for Creighton Campus Pharmacy

Creighton University’s pharmacy opened on January 9 at its new location at the University Campus of Creighton University Medical Center. The pharmacy is now called the Creighton University Campus Pharmacy.

The new 2,634-square-foot space, on the entry level floor at 2412 Cuming St., offers the same services as the current hospital location, plus expanded services in medication therapy management and prospective medication reviews.

Interprofessional Practice (IPP) will also be a cornerstone of the relocated facility. IPP is a collaborative model of patient care delivery Creighton has been developing, allowing health care providers to work with others within their profession or discipline and with people outside the profession or discipline to improve the health of patients and their families.

The pharmacy phone number is 402.449.4560.
The pharmacy is open Monday through Friday from 8:30 a.m. to 6 p.m.
Osteoporosis Treatments

Written by Ann Cabri, PharmD Candidate 2017, Creighton University School of Pharmacy & Health Professions; Mark Malesker, PharmD, FCCP, FCCP, FASHP, BCPS, Professor of Pharmacy Practice and Medicine, Creighton University School of Pharmacy & Health Professions; and Robert Recker, MD, MACP, FACE, Professor of Medicine, Chief, Division of Endocrinology, Director, Osteoporosis Research Center, Creighton University School of Medicine.

Introduction

The definition of postmenopausal osteoporosis has changed in recent years. There are three possible definitions:
1. History of a low-trauma fracture in someone, male or female, over age 50 regardless of bone density/mass,
2. a FRAX score of >3 for the hip, and/or >20 for other major fracture, or
3. a T-score (by DXA) of the total hip, or lumbar spine, of <-2.5.

Low-trauma fracture is defined as fracture occurring due to trauma less than, or equal to, a fall to the floor from a standing height, excluding fractures of the digits, face or skull. In the past, osteoporosis was thought to be due, exclusively, to low bone mass/density. However, it is now known that variation in bone density is responsible for only about 50% of the variation in risk of fracture. It is now clear that variation in mechanical quality of bone tissue, and/or its microanatomy contribute to -50% of the risk of low-trauma fracture.

Osteoporosis-related fracture is a preventable medical complication associated with significant morbidity and mortality. In the U.S., there are ~1.5 million osteoporosis-related fractures annually, where the lifetime incidence for adults over 50 years of age is 50% in women and 20% in men. In addition to imposing significant disability and morbidity, survival rates are 20% lower in patients who suffer from fracture.1 Nevertheless, bone mineral density (BMD) of the hip or spine is a strong risk factor for potential fracture. For every one-standard deviation decrease in BMD below normal, the risk for fracture increases 2-3 fold.2 Postmenopausal women have the highest risk, and treatment is generally recommended when a patient’s T-score is ≤-2.5, they have had a previous spine or hip fracture, or their FRAX score indicates significant fracture risk.

Treatments for osteoporosis include calcium and vitamin D supplements, bisphosphonates (alendronate, risedronate, ibandronate, zoledronic acid), recombinant human parathyroid hormone (teriparatide), selective estrogen receptor modulators (raloxifene), and RANK ligand inhibitors (denosumab). The safety profile of these agents is well defined, and even the most serious adverse effects are rare.3 The prevalence of osteoporosis is increasing, yet initiation of pharmacologic therapies for prevention and treatment have declined.4 The most important barrier to successful treatment is fear of possible side effects by the patient.5

Bisphosphonates have proven to be effective in reducing excessively high bone remodeling rates, improving bone mineral density, and reducing fracture risk by about 50%. Therefore, the drugs from this class are considered first-line treatment for osteoporosis. Over the past decade, the FDA has made several safety announcements pertaining to unforeseen complications associated with long-term bisphosphonate therapy. The FDA released warnings about the potential risk of osteonecrosis of the jaw in 2005, atrial fibrillation in 2007, and atypical femur fracture in 2010. News outlets also reported these findings and the public started to express growing concerns with regards to the safety of bisphosphonates. Consequently, bisphosphonate use declined by up to 50% from 2008 to 2012, in spite of the fact that these risks are extremely rare and complications have occurred mostly in cancer patients who receive doses ~12-15 times larger than osteoporosis patients.6

The purpose of this article is to address safety concerns with regards to bisphosphonates and calcium/vitamin D, and to summarize current expert opinions on prevention and treatment of osteoporosis in light of current safety and efficacy evidence.

Safety Concerns

Bisphosphonates

Bisphosphonates are the recommended first-line treatment for osteoporosis. Bisphosphonates can also be used for...
hypercalcemia due to malignancy; however, this requires significantly higher doses of bisphosphonates (12-15 times more). During randomized controlled trials, these drugs were determined to be safe while reducing fracture rates; however, some consider the safety of these agents to be controversial given post-marketing studies describing the following complications: osteonecrosis of the jaw, atrial fibrillation, atypical femur fracture, and esophageal cancer.

**Osteonecrosis of the Jaw (ONJ)**

ONJ is a rare complication reported with bisphosphonate and denosumab use. Reports suggest ONJ occurs primarily in oncology patients compared to osteoporosis patients (<15% and 0.01% respectively). Denosumab has shown incidence rates similar to high-dose bisphosphonates used in oncology patients. For comparison, incidence among the general population is <0.001%. There are no randomized controlled trials to identify true risk factors, but it is believed that individuals undergoing dental procedures or individuals who develop dental infections are at higher risk for ONJ development. In addition to dental infection, other conditions that may be significant risk factors include treatment with chemotherapy, erythropoietin therapy, renal dialysis, hypothyroidism, and diabetes. A recent meta-analysis indicated that zoledronic acid could significantly reduce fracture risk and increase bone mineral density in postmenopausal osteoporotics while serious adverse effect incidence rates were comparable to control groups. Most experts in the field of clinical osteoporosis research believe the safety risks of osteoporosis medications are greatly exaggerated. Although rarely mentioned, one feature of the purported risk of ONJ in osteoporosis patients is that the management of ONJ in osteoporotic patients is usually benign and easily tolerated compared to that in cancer patients. Delay in treating some dental problems because of ongoing osteoporosis treatment may result in greater complications than prompt treatment of the dental problem. Apical abscess comes to mind where the risk of delaying treatment can be sepsis and death.

**Atrial Fibrillation**

There is no real conclusive evidence suggesting bisphosphonates increase a patient’s risk of developing atrial fibrillation. In the HORIZON-pivotal fracture trial, more patients developed “serious” atrial fibrillation (as defined by the study) when taking zoledronic acid compared to placebo; however, the overall incidence of atrial fibrillation between the treatment and control groups were comparable. No other randomized controlled studies to date have shown a higher incidence of atrial fibrillation when comparing bisphosphonate versus placebo administration. Given the population studied in osteoporosis trials (the elderly and post-menopausal women) experts believe it is likely that these individuals developed atrial fibrillation for reasons other than bisphosphonate use.

**Atypical Femur Fracture**

Atypical femur fracture is another rare complication associated with bisphosphonate use. While more studies are needed to identify risk, a secondary analysis of three bisphosphonate randomized controlled trials found that the benefits significantly outweigh the risks. When treating 1000 women for three years with a bisphosphonate, approximately 100 fractures (number needed to treat of 10) would be prevented and only 0.3-1.4 atypical femur fractures (number needed to harm of 714-3333) would develop. While atypical femur fracture is a legitimate concern, the number of fractures prevented greatly outweighs potential atypical fracture. Atypical fractures and ONJ occur rarely in humans not on bisphosphonate or denosumab treatment.

**Esophageal Cancer**

A common side effect of oral bisphosphonates is esophagitis, particularly with alendronate, and therefore, it is recommended to take bisphosphonates with a large glass of water in the morning and patients are to remain upright for at least 30 minutes after swallowing; however, concerns about potential association with esophageal cancer was not noted until 2009. Some suspect that gastric irritation and erosive esophagitis could be plausible causes in the development of esophageal cancer. Since that time, four meta analyses have noted conflicting evidence, and therefore, there have been no conclusions made with regards to the association between bisphosphonate therapy and esophageal cancer. Experts believe the benefits outweigh the risks, but patients with other risk factors for potential development of upper gastrointestinal cancers should be evaluated individually to reassess risks and benefits. Currently, there is not enough evidence to draw hard conclusions; however, current evidence does not suggest association between bisphosphonate use and evaluation of esophageal cancer.

**Calcium and Vitamin D**

Calcium is the primary nutrient responsible for maintaining bone health. Vitamin D promotes calcium absorption by the gut and helps to maintain adequate serum calcium and phosphate concentrations. It is also necessary for normal osteoblast function in bone formation. Studies have shown that supplementing calcium and vitamin D can prevent future fractures, but these results are most evident in individuals not receiving adequate dietary calcium and vitamin D. Older systematic reviews captured data suggesting that calcium and vitamin D supplementation may reduce fracture rates, while newer analyses show inconsistent results. Calcium supplements should be taken during a meal to facilitate absorption. Individuals should also be aware of any other prescription medications that must be taken separately from calcium to prevent chelation and erratic absorption.

**Cardiovascular Risk**

Recent studies reported by social media outlets suggest that high quantities of calcium may pose a cardiovascular risk. As a result, many individuals are shying away from calcium and vitamin D supplementation; however, expert consensus groups emphasize the importance of maintaining appropriate calcium and vitamin D levels. In the most recent systematic review and meta-analysis evaluating the safety and efficacy of calcium + vitamin D, authors concluded that calcium intake from either food or supplement at levels between 2000-2500 mg/day are not associated with
cardiovascular disease risk, particularly myocardial infarction. Although there were a few trials and cohort studies included in the analysis that did show a small increase in cardiovascular risk with higher calcium intake, this increase (of approximately 10% relative risk) was not considered clinically significant by the clinician authors. The National Osteoporosis Foundation (NOF) and American Society of Preventative Cardiology (ASPC) recently convened an expert panel to evaluate the available literature and develop recommendations with regards to calcium supplementation. They propose there is moderate-quality evidence to suggest that calcium with or without vitamin D intake has no relationship to cardiovascular disease, cerebrovascular disease, mortality, or all-cause mortality in generally healthy adults; therefore, consuming the recommended daily value of calcium should be safe from a cardiovascular standpoint. NOF and ASPC recommend dietary calcium as the primary source and supplements should be utilized to correct dietary shortfalls. The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and International Foundation for Osteoporosis (IOF) also advocate for calcium and vitamin D supplementation in individuals receiving insufficient dietary quantities. They also advocate for supplementation in all patients receiving anti-osteoporosis therapy because these agents were studied and approved as adjunct therapy to calcium and vitamin D supplementation.

Evaluation of cardiovascular risk has been via secondary analyses. Further study is needed to evaluate this as a potential adverse event; however, studies to date do not suggest calcium and vitamin D contribute to adverse cardiovascular events. While more evidence is needed, evidence-based medicine advocates maintaining 2000-2500 mg/day of calcium from dietary and supplementary sources when necessary to maintain bone health.

Role of the Pharmacist
Pharmacists can help identify individuals in need of further osteoporosis workup, improve therapy compliance, and prevent fall-related complications.

Pharmacists play a crucial role in identifying patients who are at risk for osteoporotic complications. While some pharmacists are involved in a formalized screening process, all pharmacists in direct patient care settings should refer patients with significant risk for specialized osteoporosis care. Pharmacists should also encourage medication compliance and be a knowledgeable source with regards osteoporosis medication safety. Pharmacists help reinforce administration instructions unique to bisphosphonates and help ensure minimal drug interactions with calcium administration. Pharmacists can refute inaccurate media reports and assure patients that bisphosphonates and supplements are safe, efficacious, and are an important component of fracture prevention. Reassurance and education will help patients feel more comfortable taking these agents, improve compliance, and consequently optimize efficacy.

In addition to addressing specific osteoporosis-related treatment, pharmacists can help prevent falls and subsequent complications. Comprehensive drug reviews and medication therapy management are critical to minimizing fall risk. In elderly patients, particularly those who are being treated for osteoporosis, pharmacists can be vigilant in identifying unnecessary medication interactions that can predispose patients to falls, and work with prescribers to identify the risks versus benefits and help optimize medication therapy.

Conclusions
Proper utilization of pharmacologic therapy and supplementation provides an overwhelming benefit to help prevent osteoporotic-related fracture. Given the significant morbidity and mortality associated with osteoporosis and the limited evidence of medication-related complications, benefits significantly outweigh potential adverse events.

Osteoporotic-related fracture can be prevented. Pharmacists play an important role in educating the public on osteoporosis risk factors, prevention, and treatment. Pharmacists also have the opportunity to ensure safe medication administration, identify potential interactions, and prevent drug-related falls. Health care providers have a responsibility to separate fact from fiction and advocate for safe and effective osteoporosis management.

References

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